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=> d stat que
L1 41 SEA FILE=REGISTRY CALRETICULIN?/CN
L2 742 SEA FILE=HCAPLUS L1 OR ?CALRETICULIN?
L4 51 SEA FILE=HCAPLUS L2 AND (?CANCER? OR ?CARCIN? OR ?NEOPLASM? OR ?TUMOR? OR ?TUMOUR? OR ?SARCOM? OR ?LYMPHOM? OR MELANO? OR LEUKEM? OR ANGIOGEN? OR ENDOTHEL? OR GROWTH)(L)(INHIBIT? OR PREVENT? OR TREAT?)

=> d ibib abs hitrn l4 1-51

L4 ANSWER 1 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:656862 HCAPLUS
TITLE: Tumor-specific immunity and antiangiogenesis generated by a DNA vaccine encoding **calreticulin** linked to a tumor antigen
AUTHOR(S): Cheng, Wen-Fang; Hung, Chien-Fu; Chai, Chee-Yin; Hsu, Keng-Fu; He, Liangmei; Ling, Morris; Wu, T.-C.
CORPORATE SOURCE: Department of Pathology, Johns Hopkins Medical Institutions, Baltimore, MD, USA
SOURCE: J. Clin. Invest. (2001), 108(5), 669-678
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: American Society for Clinical Investigation
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Antigen-specific **cancer** immunotherapy and antiangiogenesis have emerged as two attractive strategies for **cancer treatment**. An innovative approach that combines both mechanisms will likely generate the most potent **antitumor** effect. We tested this approach using **calreticulin** (CRT), which has demonstrated the ability to enhance MHC class I presentation and exhibit an antiangiogenic effect. We explored the linkage of CRT to a model **tumor** antigen, human papilloma virus type-16 (HPV-16) E7, for the development of a DNA vaccine. We found that C57BL/6 mice vaccinated intradermally with CRT/E7 DNA exhibited a dramatic increase in E7-specific CD8+ T cell precursors and an impressive **antitumor** effect against E7-expressing **tumors** compared with mice vaccinated with wild-type E7 DNA or CRT DNA. Vaccination of CD4/CD8 double-depleted C57BL/6 mice and immunocompromised (BALB/c nu/nu) mice with CRT/E7 DNA or CRT DNA generated significant redn. of lung **tumor** nodules compared with wild-type E7 DNA, suggesting that antiangiogenesis may have contributed to the **antitumor** effect. Examn. of microvessel d. in lung **tumor** nodules and an in vivo **angiogenesis** assay further confirmed the antiangiogenic effect generated by CRT/E7 and CRT. Thus, **cancer** therapy using CRT linked to a **tumor** antigen holds promise for **treating tumors** by combining antigen-specific immunotherapy and antiangiogenesis.

REFERENCE COUNT: 54

REFERENCE(S):

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(3) Basu, S; Immunity 2001, V14, P303 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 51 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:618207 HCAPLUS

DOCUMENT NUMBER: 135:190398

TITLE: Nucleic acid markers useful for the identification, assessment, **prevention** and therapy of human **cancers**

INVENTOR(S): Roth, Frederick P.; Van Huffel, Christophe; White, James V.; Shyjan, Andrew W.

PATENT ASSIGNEE(S): Millennium Predictive Medicine, Inc., USA

SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001061048	A2	20010823	WO 2001-US5263	20010216

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-183312 P 20000217

AB The present invention is directed to the identification of markers that can be used to det. the sensitivity of cancer cells to a therapeutic agent. The present invention is also directed to the identification of therapeutic targets. Nucleic acid arrays were used to det. the level of expression of sequences (genes) found in 60 different solid tumor cancer cell lines selected form the NCI 60 cancer cell line series. Expression anal. was used to identify markers assocd. with sensitivity to certain chemotherapeutic agents.

IT **144713-90-6, Calreticulin** (human clone Ro38-1 precursor protein moiety reduced)
RL: ANT (Analyte); BOC (Biological occurrence); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(amino acid sequence; nucleic acid markers useful for the identification, assessment, **prevention** and therapy of human **cancers**)

L4 ANSWER 3 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:545510 HCAPLUS
DOCUMENT NUMBER: 135:121187
TITLE: Compositions and methods using heat-shock protein-antigen complexes to treat neurodegenerative disorders, and isolation of the complexes
INVENTOR(S): Srivastava, Pramod K.
PATENT ASSIGNEE(S): University of Connecticut Health Center, USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001052877	A1	20010726	WO 2001-US1671	20010118

W: AU, CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

PRIORITY APPLN. INFO.: US 2000-489215 A 20000121

AB The invention provides compns. comprising complexes of heat-shock proteins noncovalently or covalently linked to antigens that display the antigenicity of antigens found in cells and tissues assocd. with the pathol. of a neurodegenerative disease or disorder (e.g. Alzheimer's Disease). The compns. may be isolated from any tissue sources in which they exist, e.g. diseased human cells, non-human models for the disease or, in vitro cultured cells that express neurodegenerative disorder-assocd. antigens. The invention further provides methods for the prevention and treatment of neurodegenerative diseases or disorders using

the compns. of the invention. The invention also provides kits comprising the compns. of the invention.

L4 ANSWER 4 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:545437 HCAPLUS
DOCUMENT NUMBER: 135:142201
TITLE: Complexes of peptide-binding fragments of heat shock proteins and their use as immunotherapeutic agents
INVENTOR(S): Srivastava, Pramod K.
PATENT ASSIGNEE(S): University of Connecticut Health Center, USA
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001052791	A2	20010726	WO 2001-US1781	20010118

W: AU, CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

PRIORITY APPLN. INFO.: US 2000-488393 A 20000120
AB The present invention relates to pharmaceutical compns. comprising peptide-binding fragments of heat shock proteins (HSPs) and noncovalent complexes of peptide-binding fragments of HSPs in noncovalent assocn. with antigenic mols. The invention further relates to methods for the use of such pharmaceutical compns. as immunotherapeutic agents for the **treatment** and **prevention** of infectious diseases and **cancer**.

L4 ANSWER 5 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:473659 HCAPLUS
DOCUMENT NUMBER: 135:205729
TITLE: Microarray analysis of the in vivo effects of hypophysectomy and **growth** hormone **treatment** on gene expression in the rat
AUTHOR(S): Flores-Morales, Amilcar; Stahlberg, Nina; Tollet-Egnell, Petra; Lundeberg, Joakim; Malek, Renae L.; Quackenbush, John; Lee, Norman H.; Norstedt, Gunnar
CORPORATE SOURCE: Department of Molecular Medicine, Karolinska Institute, Stockholm, 17176, Swed.
SOURCE: Endocrinology (2001), 142(7), 3163-3176
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors used cDNA microarrays contg. 3000 different rat genes to study the consequences of severe hormonal deficiency (hypophysectomy) on the gene expression patterns in heart, liver, and kidney. Hybridization signals were seen from a majority of the arrayed cDNAs; nonetheless, tissue-specific expression patterns could be delineated. Hypophysectomy

affected the expression of genes involved in a variety of cellular functions. Between 16-29% of the detected transcripts from each tissue changed expression level as a reaction to this condition. Chronic treatment of hypophysectomized animals with human GH also caused significant changes in gene expression patterns. The study confirms previous knowledge concerning certain gene expression changes in the above-mentioned situations and provides new information regarding hypophysectomy and chronic human GH effects in the rat. Furthermore, the authors have identified several new genes that respond to GH treatment. The results represent a first step toward a more global understanding of gene expression changes in states of hormonal deficiency.

REFERENCE COUNT: 92

REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 51 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:456229 HCAPLUS

DOCUMENT NUMBER: 135:194164

TITLE: Mapping and expression pattern analysis of key components of the major histocompatibility complex class I antigen processing and presentation pathway in a representative human renal cell carcinoma cell line

AUTHOR(S): Lichtenfels, Rudolf; Ackermann, Angelika; Kellner, Roland; Seliger, Barbara

CORPORATE SOURCE: IIIrd Department of Internal Medicine, Johannes Gutenberg University, Mainz, D-55101, Germany

SOURCE: Electrophoresis (2001), 22(9), 1801-1809
CODEN: ELCTDN; ISSN: 0173-0835

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Renal cell **carcinoma** (RCC) represent approx. 5% of all **cancer** deaths. At the time of presentation, over 50% of the patients have already developed locally advanced or metastatic disease with five-year survival rates of less than 20%. Although relative resistant to conventional regimens, RCC are partially susceptible to T cell-based immunotherapy. To further develop this **treatment** modality, two-dimensional PAGE (2-D PAGE) was applied for both the mapping of the key components of the major histocompatibility complex (MHC) class I antigen processing and presentation machinery (APM) and the characterization of the constitutive and cytokine-regulated protein expression profiles in a representative human RCC cell line. The latter aspect is based on the fact, that the expression level of some of the APM components can be altered in response to interferon (IFN)-.gamma. **treatment**. Total cell lysates from untreated and IFN-.gamma.-**treated tumor** cells were sepd. on 2-D PAGE gels using broad range immobilized pH gradient (IPG) strips. Serial Western blot

analyses using sets of APM-specific antibodies were performed to target the relevant protein spots. Protein verification was mostly accomplished via peptide mass finger-printing using matrix-assisted laser desorption/ionization-mass spectrometry (MALDI-MS). To date, the majority of the APM-related components have been identified and mapped. In addn., the different protein expression profiles of untreated and IFN-.gamma.-**treated** RCC cells are under investigation.

REFERENCE COUNT: 36
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:380422 HCAPLUS
DOCUMENT NUMBER: 134:365715
TITLE: Cytokine compositions for modulating ER stress-induced cholesterol/triglyceride accumulation
INVENTOR(S): Austin, Richard C.; Werstuck, Geoff
PATENT ASSIGNEE(S): Hamilton Civic Hospitals Research Centre Inc., Can.
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001035986	A2	20010525	WO 2000-CA1372	20001116

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-166114 P 19991116

AB The present invention provides methods for **preventing** the accumulation of cholesterol/triglycerides within mammalian cells. The present methods are based upon the surprising discovery that endoplasmic reticulum (ER) stress in a cell, e.g., **endothelial** cells, smooth muscle, macrophages, and hepatic cells, leads to cholesterol/triglyceride accumulation within the cell, which cholesterol/triglyceride accumulation is often a causative factor in the development of any of a no. of conditions or diseases, such as atherosclerosis. The ER stress can be the result of any of a variety of causes, including homocysteine, viral infection, and hypoxia. Accordingly, counteracting the progression or the severity of ER stress by a cytokine, e.g., interleukin-3, can be used to

inhibit the accumulation of cholesterol/triglycerides in said cell, thereby **preventing** or lessening the severity of any of a no. of cholesterol-related diseases or conditions, e.g., atherosclerosis. In addn., the presence of ER stress in a cell can be used to diagnose a cholesterol assocd. disease, or to predict the propensity of a mammal to develop a disease.

L4 ANSWER 8 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:338762 HCAPLUS
DOCUMENT NUMBER: 134:362292
TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
INVENTOR(S): Farr, Spencer
PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165398 P 19991105
US 2000-196571 P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to det. the hypersensitivity of individuals to a given agent, such as drug or other chem., in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes assocd. with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes assocd. with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes assocd. with hypersensitivity. The expression of the genes predetd. to be assocd. with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and app. useful for identifying hypersensitivity in a subject are also disclosed.

L4 ANSWER 9 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:230502 HCAPLUS
DOCUMENT NUMBER: 134:365952
TITLE: IgA cross-reactivity between a nuclear autoantigen and wheat proteins suggests molecular mimicry as a possible pathomechanism in celiac disease
AUTHOR(S): Natter, Susanne; Granditsch, Gerhard; Reichel, Gerlinde L.; Baghestanian, Mehrdad; Valent, Peter; Elfman, Lena; Gronlund, Hans; Kraft, Dietrich; Valenta, Rudolf
CORPORATE SOURCE: Department of Pathophysiology, AKH, University of Vienna, Vienna, Austria
SOURCE: Eur. J. Immunol. (2001), 31(3), 918-928
CODEN: EJIMAF; ISSN: 0014-2980
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Celiac disease patients display IgA antibody reactivity to wheat as well as to human proteins. We used serum IgA from celiac patients and, for control purposes, from patients with Crohn's disease, ulcerative colitis and from healthy individuals to identify celiac disease-specific IgA autoantigens in nitrocellulose-blotted exts. from various human cell types (epithelial, **endothelial**, intestinal cells, fibroblasts). The pattern, recognition intensity and time course of IgA autoreactivity was monitored using serial serum samples obtained from celiac children before and under gluten-free diet. By immunoblot **inhibition** and subcellular (cytosolic, nuclear) cell fractionation we identified a 55 kDa nuclear autoantigen expressed in intestinal, **endothelial** cells and in fibroblasts which was recognized by IgA antibodies of approx. half of the celiac disease patients and cross-reacted with wheat proteins. IgA reactivity to the 55 kDa autoantigen disappeared during gluten-free diet and was **inhibited** after pre-absorption of sera with wheat proteins but not with tissue transglutaminase, previously reported as the unique celiac disease-specific autoantigen. In conclusion, we defined a novel 55 kDa celiac disease-specific nuclear IgA autoantigen which shares epitopes with wheat proteins and which is different from tissue transglutaminase and **calreticulin**. Although the newly defined autoantigen was recognized much less frequently than tissue transglutaminase, our data suggest mol. mimicry between wheat and human proteins as a possible pathomechanism for the induction and/or maintenance of mucosal tissue damage in celiac disease.
REFERENCE COUNT: 44
REFERENCE(S): (2) Brusco, G; Clin Exp Immunol 1999, V118, P371 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:150908 HCAPLUS

DOCUMENT NUMBER: 134:309402
TITLE: Characterization of the major histocompatibility complex class I deficiencies in B16 melanoma cells
AUTHOR(S): Seliger, Barbara; Wollscheid, Ursula; Momburg, Frank; Blankenstein, Thomas; Huber, Christoph
CORPORATE SOURCE: Johannes Gutenberg Universitat, III. Medizinische Klinik, Mainz, 55131, Germany
SOURCE: Cancer Res. (2001), 61(3), 1095-1099
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The murine B16 **melanoma** system represents an important in vivo model for the evaluation of T cell-based immunization and vaccination strategies, although deficient MHC class I surface expression has been identified in these cells. The authors postulate here that the MHC class I-deficient phenotype of B16 **melanoma** cells is attributable to down-regulation or the loss of the expression and function of multiple components of the MHC class I antigen-processing pathway, including the peptide transporter assocd. with antigen processing, the proteasome subunits LMP2, LMP7, and LMP10, PA28.alpha. and -.beta., and the chaperone tapasin. In contrast, calnexin, **calreticulin**, ER60, and protein disulfide isomerase expression are unaltered or only marginally suppressed in these cells. The level of down-regulation of the components of the antigen-processing pathway is either transcriptionally or post-transcriptionally controlled and could be cor. in all cases by IFN-.gamma. **treatment**, which also reconstituted MHC class I surface expression. Thus, B16 **melanoma** cells can be used as a model for the characterization of the mechanisms underlying the coordinated dysregulation of the antigen-processing components, which should provide new insights into the development of **tumors** and the factors controlling this process.

REFERENCE COUNT: 38
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:105937 HCAPLUS
DOCUMENT NUMBER: 134:158091
TITLE: Activation of extracellular signal-regulated kinases (ERKs) defines the first phase of 1,25-dihydroxyvitamin D3-induced differentiation of HL60 cells
AUTHOR(S): Wang, Xuening; Studzinski, George P.
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, UMDNJ-New Jersey Medical School, Newark, NJ, 07103, USA
SOURCE: J. Cell. Biochem. (2000), 80(4), 471-482
CODEN: JCEBD5; ISSN: 0730-2312

PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Activation of ERK1 and ERK2 protein kinases has been implicated in diverse cellular processes, including the control of cell proliferation and cell differentiation. In human myeloblastoid **leukemia** HL60 cells rapid (.apprx.15 min) but transient activation of ERK1/2 has been reported following induction of macrophage/monocyte differentiation by phorbol esters, or by very high (10-6 M) concns. of 1,25-dihydroxyvitamin D3 (1,25D3), while retinoic acid-induced granulocytic differentiation was accompanied by sustained activation of ERK1/2. The authors report that monocytic differentiation of HL60 cells induced by moderate (10-9 to 10-7 M) concns. of 1,25D3 could be divided into at least two stages. In the first phase, which lasts 24-48h, the cells continued in the normal cell cycle while expressing markers of monocytic phenotype, such as CD14. In the next phase the onset of G1 cell cycle block became apparent and expression of CD11b was prominent, indicating a more mature myeloid phenotype. The first phase was characterized by high levels of ERKs activated by phosphorylation, and these decreased as the cells entered the second phase, while the levels of p27/Kip1 increased at that time. Serum-starved or PD98059-**treated** HL60 cells had reduced **growth** rate and slower differentiation, but the G1 block also coincided with decreased levels of activated ERK1/2. The data suggest that the MEK/ERK pathway maintains cell proliferation during 1,25D3-induced monocytic differentiation of HL60 cells, but that ERK1/2 activity becomes suppressed during the later stages of differentiation, and the consequent G1 block leads to "terminal" differentiation.
REFERENCE COUNT: 42
REFERENCE(S): (1) Alberola-Ila, J; Nature 1995, V373, P620 HCAPLUS
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(5) Blenis, J; Proc Natl Acad Sci 1993, V90, P5889 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:831887 HCAPLUS
DOCUMENT NUMBER: 134:111402
TITLE: Aluminum-induced 1.fwdarw.3-.beta.-D-glucan inhibits cell-to-cell trafficking of molecules through plasmodesmata. A new mechanism of aluminum toxicity in plants
AUTHOR(S): Sivaguru, Mayandi; Fujiwara, Toru; Samaj, Josef; Baluska, Frantisek; Yang, Zhenming; Osawa, Hiroki; Maeda, Takanori; Mori, Tomoko; Volkmann, Dieter; Matsumoto, Hideaki
CORPORATE SOURCE: Research Institute for Bioresources, Okayama University, Kurashiki, 710-0046, Japan
SOURCE: Plant Physiol. (2000), 124(3), 991-1005
CODEN: PLPHAY; ISSN: 0032-0889
PUBLISHER: American Society of Plant Physiologists
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Symplastic intercellular transport in plants is achieved by plasmodesmata (PD). These cytoplasmic channels are well known to interconnect plant cells to facilitate intercellular movement of water, nutrients, and signaling mols. including hormones. However, it is not known whether Al may affect this cell-to-cell transport process, which is a crit. feature for roots as organs of nutrient/water uptake. The authors have microinjected the dye lucifer yellow carbohydrazide into peripheral root cells of an Al-sensitive wheat (Triticum aestivum cv Scout 66) either before or after Al **treatment** and followed the cell-to-cell dye-coupling through PD. Here, the authors show that the Al-induced root **growth inhibition** is closely assocd. with the Al-induced blockage of cell-to-cell dye coupling. Immunofluorescence combined with immuno-electron microscopic techniques using monoclonal antibodies against 1.fwdarw.3-.beta.-D-glucan (callose) revealed circumstantial evidence that Al-induced callose deposition at PD may be responsible for this blockage of symplastic transport. Use of 2-deoxy-D-glucose, a callose synthesis **inhibitor**, allowed the authors to demonstrate that a redn. in callose particles correlated well with the improved dye-coupling and reduced root **growth inhibition**. While assessing the tissue specificity of this Al effect, comparable responses were obtained from the dye-coupling pattern in tobacco (Nicotiana tabacum) mesophyll cells. Analyses of the Al-induced expression of PD-assocd. proteins, such as **calreticulin** and unconventional myosin VIII, showed enhanced fluorescence and co-localizations with callose deposits. These results suggest that Al signal-mediated localized alterations to calcium homeostasis may drive callose formation and PD closure. Thus, extracellular Al-induced callose deposition at PD could effectively block symplastic transport and communication in higher plants.

REFERENCE COUNT: 75

REFERENCE(S):

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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 51 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:820413 HCAPLUS

DOCUMENT NUMBER: 134:365408

TITLE: Coordinate downregulation of multiple MHC class I antigen processing genes in chemical-induced murine tumor cell lines of distinct origin

AUTHOR(S): Seliger, B.; Wollscheid, U.; Momburg, F.; Blankenstein, T.; Huber, C.

CORPORATE SOURCE: Johannes Gutenberg Universitat, III. Medizinische Klinik, Mainz, 55131, Germany

SOURCE: Tissue Antigens (2000), 56(4), 327-336
CODEN: TSANA2; ISSN: 0001-2815

PUBLISHER: Munksgaard International Publishers Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In murine **tumor** cell lines, downregulation of MHC class I surface expression has been frequently detected, but the underlying mol. mechanisms of such deficiencies have not been defined. In this study, murine **tumor** cell lines of different histol. derived from spontaneous or from chem.-induced **tumors** were analyzed for the expression of multiple components of the major histocompatibility complex (MHC) class I antigen-processing machinery (APM), including the peptide transporter TAP, the interferon (IFN)-.gamma. inducible proteasome subunits and several chaperones. The **tumor** cell lines analyzed demonstrated a heterogeneous expression pattern of various APM components. In comparison to control cells an impaired coordinated expression of at least three APM components was detected. In particular, extensive APM deficiencies were found in cell lines derived from chem.-induced **tumors**. A strong coordinated downregulation of expression and/or function of TAP, the low mol. wt. proteins (LMP) subunits, the proteasome activator PA28 and/or tapasin was found in 5 of 10 **tumor** cells, which was assocd. with impaired MHC class I surface expression. In contrast, the expression of .beta.2-microglobulin (.beta.2-m), PA28.beta., the constitutive proteasome subunits X, Y, Z and of the chaperones calnexin, **calreticulin**, ER60 and phospho disulfide isomerase (PDI) was unaltered or only weakly decreased. The deficient expression of APM components could be cor. by IFN-.gamma. **treatment**, which also reconstituted MHC class I surface expression. However, impaired expression of APM mols. appears not to be the only cause of abnormal MHC class 1 expression, since it could neither be cor. by the addn. of exogenous MHC class I binding peptides nor by incubation at low temp. These results suggest that one major mechanism of murine **tumor** cells, in particular chem.-induced **tumors**, to evade the immune system is the combined dysregulation of various APM components and other factors, which still have to be identified.

REFERENCE COUNT: 49
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:706994 HCAPLUS
DOCUMENT NUMBER: 133:286473
TITLE: Compositions and methods for producing platelets and/or proplatelets from megakaryocytes
INVENTOR(S): Loscalzo, Joseph; Battinelli, Elisabeth M.
PATENT ASSIGNEE(S): Trustees of Boston University, USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000057891	A1	20001005	WO 2000-US6436	20000330

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-126854 P 19990330
OTHER SOURCE(S): MARPAT 133:286473

AB The present invention describes novel compns. and methods to enhance the in vitro and in vivo prodn. of platelets and/or proplatelets from megakaryocytes. The present invention describes compns. comprising megakaryocytes, nitric oxide donors (i.e. compds. that donate, transfer or release nitric oxide, elevate endogenous levels of **endothelium** -derived relaxing factor, stimulate endogenous synthesis of nitric oxide or are substrates for nitric oxide synthase), and, optionally, at least one thrombopoiesis stimulating factor. The thrombopoiesis stimulating factor is preferably thrombopoietin. The nitric oxide donor is preferable S-nitrosoglutathione. The present invention also describes compns. comprising at least one nitric oxide donor and at least one thrombopoiesis stimulating factor. The present invention also provides methods for **treating** and/or **preventing** blood platelet disorders, and for producing platelets and/or proplatelets in vitro and in vivo. The compds. and/or compns. of the present invention can be provided in the form of a pharmaceutical kit.

REFERENCE COUNT: 3
REFERENCE(S):
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(2) Bolton; US 5834030 A 1998 HCAPLUS
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L4 ANSWER 15 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:608612 HCAPLUS
DOCUMENT NUMBER: 133:206756
TITLE: Compositions and methods using complexes of **calreticulin** and antigenic molecules
INVENTOR(S): Gilboa, Eli; Nair, Smita K.; Nicchitta, Christopher V.
PATENT ASSIGNEE(S): Duke University, USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050080	A1	20000831	WO 2000-US4565	20000223

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,

IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-261473 A 19990226

AB A method of eliciting an immune response in a vertebrate subject. The method includes the administration to a vertebrate subject of a compn. including an amt. of a purified complex including **calreticulin** bound to an antigenic mol. to elicit an immune response to the antigenic mol. in the vertebrate subject. Therapeutic methods, compns. and kits are also disclosed wherein the elicited immune response is utilized as a **treatment** for **cancer** and for infectious diseases.

L4 ANSWER 16 OF 51 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:521385 HCAPLUS
DOCUMENT NUMBER: 133:217893
TITLE: Unliganded and liganded estrogen receptors protect against cancer invasion via different mechanisms
AUTHOR(S): Platet, Nadine; Cunat, Severine; Chalbos, Dany; Rochefort, Henri; Garcia, Marcel
CORPORATE SOURCE: Institut National de la Sante et de la Recherche Medicale Unite Hormones et Cancer (U148) and Universite de Montpellier I, Montpellier, 34090, Fr.
SOURCE: Mol. Endocrinol. (2000), 14(7), 999-1009
CODEN: MOENEN; ISSN: 0888-8809
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB While estrogens are mitogenic in breast **cancer** cells, the presence of estrogen receptor .alpha. (ER.alpha.) clin. indicates a favorable prognosis in breast **carcinoma**. To improve our understanding of ER.alpha. action in breast **cancer**, we used an original in vitro method, which combines transient transfection and Matrigel invasion assays to examine its effects on cell invasiveness. ER.alpha. expression in MDA-MB-231 breast **cancer** cells reduced their invasiveness by 3-fold in the absence of hormone and by 7-fold in its presence. Integrity of hormone and DNA-binding domains and activating function 2 were required for estradiol-induced **inhibition**, suggesting that transcriptional activation of estrogen target genes was involved. In contrast, these domains were dispensable for hormone-independent **inhibition**. Anal. of deletion mutants of ER.alpha. indicated that amino acids 179-215, contg. the N-terminal zinc finger of the DNA-binding domain, were required for ligand-independent receptor action. Among different members of the nuclear receptor family, only unliganded ER.alpha. and ER.beta. reduced invasion. **Calreticulin**, a Ca2+-binding protein that could interact with amino acids 206-211 of ER.alpha., reversed hormone-independent ER.alpha. **inhibition** of invasion. However, since **calreticulin** alone also **inhibited** invasion, we propose that this protein probably **prevents** ER.alpha. interaction with another unidentified invasion-regulating factor. The **inhibitor** role of

the unliganded ER was also suggested in three ER.alpha.-pos. cell lines, where ER.alpha. content was inversely correlated with cell migration. We conclude that ER.alpha. protects against **cancer** invasion in its unliganded form, probably by protein-protein interactions with the N-terminal zinc finger region, and after hormone binding by activation of specific gene transcription.

REFERENCE COUNT: 50
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:351546 HCAPLUS
DOCUMENT NUMBER: 133:13447
TITLE: A regulatory element in genes for chaperonins of the endoplasmic reticulum involved in stress induction of gene expression
INVENTOR(S): Haze, Kyosuke; Yoshida, Hiderou; Mori, Kazutoshi; Yanagi, Hideki; Yura, Takashi
PATENT ASSIGNEE(S): HSP Research Institute, Inc., Japan
SOURCE: PCT Int. Appl., 157 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000029429	A2	20000525	WO 1999-JP6305	19991112
WO 2000029429	A3	20001109		
W: CA, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 2001054391	A2	20010227	JP 1999-321743	19991111
EP 1131435	A2	20010912	EP 1999-972220	19991112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: JP 1998-324227 A 19981113
JP 1999-163112 A 19990609
WO 1999-JP6305 W 19991112

AB A regulatory element that plays a role in the induction and repression of expression of genes for chaperonins of the endoplasmic reticulum is described. The element can be used to regulate the expression of foreign genes in animal cells. The element, ERSE (endoplasmic reticulum stress element) is regulated by the transcription factors ATF-6 and CREB-BP. It is expected to be applied to **treatment** or prophylaxis of **cancers**, arteriosclerosis, cystic fibrosis, ischemic diseases, wounds or ulcers. The element was identified in the human GRP78 promoter by deletion and point mutation anal. Similar sequences were found in the

genes for GRP94 and **calreticulin**. Genes encoding transcription factors interacting with ERSE were identified using single hybrid anal. ATF6 was found to be synthesized as an inactive precursor that was activated by proteolytic cleavage during stress. CREB-BP was also found to be synthesized as an inactive precursor that was activated by proteolytic cleavage during stress. N-terminal deletion derivs. of ATF6 and CREB-RP suppress ERSE-dependent gene expression.

L4 ANSWER 18 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:242976 HCAPLUS
DOCUMENT NUMBER: 133:236554
TITLE: Immunoprotective activities of multiple chaperone proteins isolated from murine B-cell leukemia/lymphoma
AUTHOR(S): Graner, Michael; Raymond, Amy; Romney, Davis; He, Lin; Whitesell, Luke; Katsanis, Emmanuel
CORPORATE SOURCE: Department of Pediatrics, Steele Memorial Children's Research Center, University of Arizona, Tucson, AZ, 85724-5073, USA
SOURCE: Clin. Cancer Res. (2000), 6(3), 909-915
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Although the use of **tumor**-derived heat shock/chaperone proteins (HSPs) as **anticancer** vaccines is gaining wider study and acceptance, there have thus far been no reports concerning chaperone **antitumor** activities against disseminated hematol. malignancies. We have devised an efficient and effective method for purifn. of the chaperone proteins grp94/gp96, HSP90, HSP70, and **calreticulin** from harvested A20 murine **leukemia/lymphoma** **tumor** material. We have demonstrated that these purified proteins, when used as vaccines, can induce potent and specific immunity against a lethal **tumor** challenge. Individual chaperone proteins were differentially effective in their abilities to provide immune protection. The increase in survival generated by the most effective chaperone vaccine, HSP70, resulted from at least a 2-log redn. in **tumor** burden. Syngeneic granulocyte macrophage colony-stimulating factor producing fibroblasts were injected at the site of vaccination in an attempt to augment the immune response. Surprisingly, localized granulocyte macrophage colony-stimulating factor prodn. **inhibited** the protective effects of chaperone vaccination. These studies provide evidence that chaperone proteins can be isolated from B-cell **tumors** and used effectively to immunize against disseminated lymphoid malignancies.
REFERENCE COUNT: 40
REFERENCE(S): (1) Arnold, D; J Exp Med 1995, V182, P885 HCAPLUS
(2) Arnold-Schild, D; J Immunol 1999, V162, P3757 HCAPLUS
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(4) Bausero, M; J Immunother 1996, V19, P113 HCAPLUS
(5) Bronte, V; J Immunol 1999, V162, P5728 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 51 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:241470 HCAPLUS
DOCUMENT NUMBER: 132:288763
TITLE: Use of **calreticulin** and **calreticulin** fragments to **inhibit endothelial** cell **growth** and **angiogenesis**, and suppress **tumor growth**
INVENTOR(S): Tosato, Giovanna; Pike, Sandra; Yao, Lei
PATENT ASSIGNEE(S): The Government of the United States of America, Represented by the Secretary, USA
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000020577	A1	20000413	WO 1999-US23240	19991005
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, ZA, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9962917	A1	20000426	AU 1999-62917	19991005

PRIORITY APPLN. INFO.: US 1998-103438 P 19981006
WO 1999-US23240 W 19991005

AB Methods for **inhibiting endothelial** cell **growth** and **angiogenesis** and for suppressing **tumor growth** using **calreticulin**, fragments of **calreticulin**, and variants of **calreticulin** are provided. Such methods are useful for the **treatment** of **cancer** and diseases assocd. with unwanted **angiogenesis**, e.g., chronic retinal detachment. Thus, **calreticulin** was shown to exhibit three previously uncharacterized biol. activities. First, **calreticulin inhibited endothelial** cell **growth** while having little or no effect on the **growth** of non-**endothelial** cells. Second, **calreticulin inhibited angiogenesis**. Third, **calreticulin inhibited tumor growth**, including **growth** of Burkitt's **lymphoma**, breast **adenocarcinoma**, colon **carcinoma**, lung **carcinoma**, **melanoma**, **rhabdomyosarcoma**, promyelomonocytic **lymphoma**, Wilm's **tumor**, and neuroblastoma. Certain fragments of **calreticulin**, e.g., **calreticulin** lacking the N-terminal 120 amino acids, the N-terminal domain (amino acids 1-180), and fragments of this N-terminal domain, were found to share these activities.

IT **144713-91-7, Calreticulin** (human clone Ro38-1 protein moiety reduced)

RL: BAC (Biological activity or effector, except adverse); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; use of **calreticulin** and **calreticulin** fragments to **inhibit endothelial** cell **growth** and **angiogenesis**, and suppress **tumor growth**)

IT **144713-90-6, Calreticulin** (human clone Ro38-1 precursor protein moiety reduced)
RL: PRP (Properties)
(unclaimed protein sequence; use of **calreticulin** and **calreticulin** fragments to **inhibit endothelial** cell **growth** and **angiogenesis**, and suppress **tumor growth**)

REFERENCE COUNT: 11
REFERENCE(S):
(1) Dai, E; ARTERIOSCLEROSIS, THROMBOSIS AND VASCULAR BIOLOGY 1997, V17(11), P2359 HCAPLUS
(2) Dedhar, S; CA 2140814 A 1996 HCAPLUS
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(4) Kishore, U; BIOCHEMICAL JOURNAL 1997, V322(2), P543 HCAPLUS
(7) Pike, S; BLOOD 1999, V94(7), P2461 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:134362 HCAPLUS
DOCUMENT NUMBER: 132:291275
TITLE: Genes dependent on zebrafish cyclops function identified by AFLP differential gene expression screen
AUTHOR(S): Rubinstein, Amy L.; Lee, Danny; Luo, Rushu; Henion, Paul D.; Halpern, Marnie E.
CORPORATE SOURCE: Department of Embryology, Carnegie Institution of Washington, Baltimore, MD, 21210, USA
SOURCE: Genesis (N. Y.) (2000), 26(1), 86-97
CODEN: GNESFY; ISSN: 1526-954X
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Zebrafish cyclops (cyc) encodes a transforming **growth** factor .beta. (TGF.beta.) signaling factor closely related to mouse Nodal. By comparing amplified fragment length polymorphisms (AFLP) from cyc mutant and wildtype cDNA pools, we devised a differential gene expression screen to isolate genes whose expression is dependent on Cyc signaling. We report 2 genes not previously described in the zebrafish that were identified using this approach. The 1st gene, crestin, is expressed predominantly in premigratory and migrating neural crest cells during somitogenesis stages. Crestin expression is reduced in cyc mutants initially but recovers by late somitogenesis. The 2nd gene encodes the zebrafish homolog of the calcium-binding protein, **calreticulin**. Zebrafish **calreticulin** is highly expressed in the hatching gland and in the floor plate, tissues that are affected in cyc mutants. During gastrulation, **calreticulin** transcripts are found in the dorsal mesendoderm, in the same cells that express the cyc gene. Expression is reduced in cyc mutants and is abolished by the one-eyed pinhead (oep) mutation that is presumed to **prevent** Nodal signaling. The

identification of **calreticulin** suggests that a differential screen between wild-type and mutant cDNA is a useful approach to reveal regulation of unexpected gene expression in response to cellular signals.

IT **264868-11-3, Calreticulin** (Danio rerio)
RL: BOC (Biological occurrence); BPR (Biological process); MFM (Metabolic formation); PRP (Properties); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PROC (Process)
(amino acid sequence; **calreticulin** and crestin protein sequence and cyclops-regulated expression in zebrafish embryos)

REFERENCE COUNT: 75
REFERENCE(S):
(2) Bachem, C; Plant J 1996, V9, P745 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:644147 HCAPLUS
DOCUMENT NUMBER: 131:331844
TITLE: **Calreticulin** and **calreticulin** fragments are **endothelial** cell **inhibitors** that suppress **tumor growth**
AUTHOR(S): Pike, Sandra E.; Yao, Lei; Setsuda, Joyce; Jones, Karen D.; Cherney, Barry; Appella, Ettore; Sakaguchi, Kazuyasu; Nakhasi, Hira; Atreya, Chintamani D.; Teruya-Feldstein, Julie; Wirth, Peter; Gupta, Ghanshyam; Tosato, Giovanna
CORPORATE SOURCE: Center for Biologics Evaluation and Research, Rockville, MD, 20852, USA
SOURCE: Blood (1999), 94(7), 2461-2468
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several **angiogenesis inhibitors** are fragments of larger proteins that are themselves not active as **angiogenesis inhibitors**. Vasostatin, the N-terminal domain of **calreticulin** inclusive of amino acids 1-180, is an **angiogenesis inhibitor** that exerts **antitumor** effects in vivo. In the present study, we examd. whether the full-length **calreticulin** mol. shares the antiangiogenic and **antitumor** activities of vasostatin. Similar to vasostatin, **calreticulin** selectively **inhibited endothelial** cell proliferation in vitro, but not cells of other lineages, and suppressed **angiogenesis** in vivo. When inoculated into athymic mice, **calreticulin inhibited** Burkitt **tumor growth** comparably with vasostatin. **Calreticulin** lacking the N-terminal 1-120 amino acids **inhibited endothelial** cell proliferation in vitro and Burkitt **tumor growth** in vivo comparably with vasostatin. An internal **calreticulin** fragment encompassing amino acids 120-180 also **inhibited**

endothelial cell proliferation in vitro and **angiogenesis** in vivo comparably with **calreticulin** and vasostatin. These results suggest that the antiangiogenic activities of vasostatin reside in a domain that is accessible from the full-length **calreticulin** mol. and localize to **calreticulin** N-terminal amino acids 120-180. Thus, **calreticulin** and **calreticulin** fragments are **inhibitors** of **angiogenesis** that directly target **endothelial** cells, **inhibit angiogenesis**, and suppress **tumor growth**. This information may be crit. in designing targeted **inhibitors** of pathol. **angiogenesis** that underlies **cancer** and other diseases.

REFERENCE COUNT: 41

REFERENCE(S):
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(5) Burns, K; FEBS Lett 1993, V318, P181 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 51 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:561437 HCAPLUS
DOCUMENT NUMBER: 132:77347

TITLE: Generation of a monoclonal antibody against human **calreticulin** by immunization with a recombinant **calreticulin** fusion protein: application in paraffin-embedded sections

AUTHOR(S): Cavill, Dana; Macardle, Peter J.; Beroukas, Dimitra; Kinoshita, Gentaro; Stahl, Jurgen; McCluskey, James; Gordon, Tom P.
CORPORATE SOURCE: Departments of Immunology, Allergy & Arthritis, University of Melbourne, Victoria, Australia

SOURCE: Appl. Immunohistochem. Mol. Morphol. (1999), 7(2), 150-155
CODEN: AIMMFN
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Calreticulin** (CR) is a highly conserved, calcium-binding protein with a diverse functional repertoire located primarily in the endoplasmic reticulum (ER). A murine monoclonal antibody (mAb) reactive with human CR was produced by immunizing with a maltose-binding protein-CR fusion protein expressed in Escherichia coli. This mAb (FMC75) bound recombinant and native human 60-kDa CR on Western blots but, unlike a polyclonal anti-CR antibody, did not cross-react with mouse CR. FMC75 gave a staining pattern identical to that of the polyclonal antibody on confocal microscopy of cultured cells and was pos. on microwave-**treated** tissue sections embedded in paraffin. Immunohistochem. anal. of a range of normal tissues confirmed the widespread expression of CR, notably in parenchymal epithelial cells, neurons, **endothelial** cells, and lymphocytes, predominantly of B-cell origin. The pattern of staining was cytoplasmic, not nuclear. Only weak staining was found in stromal cells. This first mAb to be produced against human CR will be a valuable reagent for studying the expression of CR and its putative role in autoimmune disease and malignancy. Recombinant fusion proteins in which the target

protein is fused with a foreign moiety may be useful immunogens for breaking tolerance and generating mAbs against extremely conserved proteins such as CR.

REFERENCE COUNT: 9

REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:532898 HCAPLUS
DOCUMENT NUMBER: 131:269858
TITLE: Roles of **calreticulin** and calnexin during mucin synthesis in LS180 and HT29/A1 human colonic adenocarcinoma cells
AUTHOR(S): McCool, Dorothy J.; Okada, Yoshio; Forstner, Janet F.; Forstner, Gordon G.
CORPORATE SOURCE: Research Institute. The Hospital for Sick Children and the Department of Biochemistry, University of Toronto, Toronto, ON, M5G 1X8, Can.
SOURCE: Biochem. J. (1999), 341(3), 593-600
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mol. chaperones are presumed to assoc. with large secretory mucin glycoproteins during their synthesis in the endoplasmic reticulum (ER), but have not been identified to date. We decided to look for possible involvement of the chaperones **calreticulin** (CRT) and calnexin (CLN) during synthesis of two similar gastrointestinal mucins, MUC2 and MUC5AC. Pulse-chase labeling of MUC2 and MUC5AC with [35S]methionine/cysteine ([35S]Promix) was performed using LS180 and HT29/A1 colonic **carcinoma** cell lines and was followed by immunopptn. with anti-mucin and anti-chaperone antibodies. The pptd. labeled mucin precursors were analyzed by SDS-PAGE and autoradiog. Using antibodies specific for each mucin, newly synthesized monomeric precursors of both MUC2 and MUC5AC were detected after a 15 min pulse and then disappeared as oligomers were formed during a 2 h chase period. Only homo-oligomers of MUC2 and MUC5AC were present in the cells. Using anti-CRT, the MUC2 monomeric precursor and oligomer were co-pptd. from both cell lines after a 15 min pulse and the oligomer less strongly after a 0.5 h chase, but there was little co-pptn. after a 2 h chase. At this time, MUC2 immunopptd. by anti-MUC2 was completely oligomerized and was endo-.beta.-N-acetylglucosaminidase-resistant, indicating that the mucin had reached the Golgi region. MUC2 co-pptd. with CRT at zero time and 0.5 h was endo-.beta.-N-acetylglucosaminidase-sensitive; therefore CRT must have assocd. with MUC2 in the ER. **Treatment** with tunicamycin (TUN) diminished the binding of MUC2 to CRT, suggesting a requirement for initial N-glycan addn. during this process. Using anti-CLN, only a weak co-pptn. of MUC2, compared with that seen with anti-CRT, was detected in

LS180 cells. In contrast with the findings for MUC2, there was no co-pptn. of MUC5AC with CRT or CLN from either cell line at the various time points. In conclusion, CRT and CLN appear to be involved in MUC2 synthesis at the stage of folding and oligomerization in the ER. Since no interaction of the chaperones with MUC5AC was detected at a similar stage of synthesis, these two structurally similar secretory mucins seem to have different chaperone requirements in the ER.

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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:369691 HCAPLUS
DOCUMENT NUMBER: 131:142586
TITLE: Ligand-specific, transient interaction between integrins and **calreticulin** during cell adhesion to extracellular matrix proteins is dependent upon phosphorylation/dephosphorylation events
AUTHOR(S): Coppolino, Marc G.; Dedhar, Shoukat
CORPORATE SOURCE: Department of Cell Biology, Hospital for Sick Children, Toronto, ON, M5G 1X8, Can.
SOURCE: Biochem. J. (1999), 340(1), 41-50
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB As transmembrane heterodimers, integrins bind to both extracellular ligands and intracellular proteins. We are currently investigating the interaction between integrins and the intracellular protein **calreticulin**. A prostatic **carcinoma** cell line (PC-3) was used to demonstrate that **calreticulin** can be found in the .alpha.3 immunoppts. of cells plated on collagen type IV, but not when plated on vitronectin. Conversely, .alpha.v immunoppts. contained **calreticulin** only when cells were plated on vitronectin, i.e. not when plated on collagen IV. The interactions between these integrins and **calreticulin** were independent of actin cytoskeleton assembly and were transient, being maximal approx. 10-30 min after the cells came into contact with the substrates prior to complete cell spreading and formation of firm adhesive contacts. We demonstrate that okadaic acid, an **inhibitor** of intracellular serine/threonine protein phosphatases, **inhibited** the .alpha.3.beta.1-mediated adhesion of PC-3 cells to collagen IV and the .alpha.2.beta.1-mediated attachment of Jurkat cells to collagen I. This **inhibition** by okadaic acid was accompanied by **inhibition** of the ligand-specific interaction of **calreticulin** with the resp. integrins in the two cell types. Addnl., we found that pharmacol. **inhibition** of mitogen-activated protein kinase kinase (MEK) resulted in prolongation of the **calreticulin**-integrin interaction, and enhancement of PC-3 cell attachment to collagen IV. We conclude that **calreticulin** interacts transiently with integrins during cell attachment and spreading.

This interaction depends on receptor occupation, is ligand-specific, and can be modulated by protein phosphatase and MEK activity.

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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 51 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:273044 HCAPLUS

DOCUMENT NUMBER: 131:57183

TITLE: **Calreticulin** expression is associated with androgen regulation of the sensitivity to calcium ionophore-induced apoptosis in LNCaP prostate cancer cells

AUTHOR(S): Zhu, Ning; Wang, Zhou

CORPORATE SOURCE: Department of Urology, Northwestern University Medical School, Chicago, IL, 60611, USA

SOURCE: Cancer Res. (1999), 59(8), 1896-1902
CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: AACR Subscription Office

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Calreticulin** has been identified previously as one of the androgen-response genes in the prostate. The role of **calreticulin** in androgen action was studied using androgen-sensitive LNCaP and androgen-insensitive PC-3 human prostate **cancer** cell lines. **Calreticulin** appears to be a primary androgen-response gene in cultured LNCaP cells because androgen induction of **calreticulin** mRNA resists protein synthesis **inhibition**. **Calreticulin** is a high capacity intracellular Ca2+ binding protein, suggesting that **calreticulin** expression is likely to be assocd. with the intracellular Ca2+ buffering capacity that could regulate the sensitivity to cytotoxic intracellular Ca2+ overload. As expected, androgen protects androgen-sensitive LNCaP but not androgen-insensitive PC-3 cells from cytotoxic intracellular Ca2+ overload induced by Ca2+ ionophore A23187. To provide evidence for the role of **calreticulin** in reducing cytotoxic effect of Ca2+ influx in prostatic cells, we have shown that **calreticulin** antisense oligonucleotide down-regulates **calreticulin** protein level and significantly increases the sensitivity to A23187-induced apoptosis in both LNCaP and PC-3 cells. Furthermore, **calreticulin** antisense oligonucleotide reverses the androgen-induced resistance to A23187 in LNCaP cells. The above observations collectively suggest that **calreticulin** mediates androgen regulation of the sensitivity to Ca2+ ionophore-induced apoptosis in LNCaP cells.

REFERENCE COUNT: 29

REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 26 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:244758 HCAPLUS
DOCUMENT NUMBER: 130:280309
TITLE: Proteins and nucleic acids associated with human prostate cancer and methods for immunotherapy and immunodiagnosis of prostate cancer
INVENTOR(S): Reed, Steven G.; Dillon, Davin C.; Twardzik, Daniel R.; Mitcham, Jennifer L.
PATENT ASSIGNEE(S): Corixa Corporation, USA
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9918210	A2	19990415	WO 1998-US21166	19981007
WO 9918210	A3	19990805		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6034218	A	20000307	US 1997-946026	19971007
AU 9896893	A1	19990427	AU 1998-96893	19981007

PRIORITY APPLN. INFO.:
US 1997-946026 A 19971007
US 1996-616745 B2 19960315
US 1996-633840 B2 19960411
US 1998-102679 A 19980623
WO 1998-US21166 W 19981007

AB Compds. and methods for **treating** and diagnosing prostate **cancer** are provided. The inventive compds. include polypeptides contg. at least a portion of a prostate protein. Polypeptide fragments and their encoding cDNAs were isolated and characterized from a suitable human prostate **adenocarcinoma** cell line, such as LnCap.fgc (ATCC 1740-CRL), by screening with human, rat, and monkey prostatitis sera or with prostate **tumor**-specific monoclonal antibodies. Vaccines and pharmaceutical compns. for immunotherapy of prostate **cancer** comprising such polypeptides or DNA mols. encoding such polypeptides are also provided. The inventive polypeptides may also be used to generate antibodies useful for the diagnosis and monitoring of prostate **cancer**. Nucleic acid sequences for prepg. probes, primers, and

polypeptides are also provided.

L4 ANSWER 27 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:96269 HCAPLUS
DOCUMENT NUMBER: 130:148717
TITLE: Pharmaceutical compositions containing proteins or peptides for modulating hormone responsiveness
INVENTOR(S): Dedhar, Shoukat; Doersen, Claus-Jens Walter; Mazur, Adam Weislaw
PATENT ASSIGNEE(S): Can.
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9905172	A2	19990204	WO 1998-CA715	19980724
WO 9905172	A3	19990415		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 5854202	A	19981229	US 1995-377432	19950124
AU 9885251	A1	19990216	AU 1998-85251	19980724
EP 1001986	A2	20000524	EP 1998-936040	19980724
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 9945861	A1	19991028	AU 1999-45861	19990901

PRIORITY APPLN. INFO.:
US 1995-377432 A2 19950124
US 1997-900241 A2 19970724
AU 1995-39203 A3 19951123
WO 1998-CA715 W 19980724

OTHER SOURCE(S): MARPAT 130:148717

AB This invention relates to isolated and purified proteins, such as **calreticulin** and mimetics and **inhibitors** of **calreticulin**, for a novel use of modulating hormone responsiveness. These proteins are useful in gene therapy and in manufg. pharmaceuticals for **treating** a variety of diseases, including **cancer**, osteoporosis and chronic inflammatory disease. The proteins include or bind to an amino acid sequence [SEQ ID NO: 1] KXFFX1R (X = G, A, V; X1 = K, R). This sequence is present in the DNA-binding domain, and is crit. for the DNA binding activity, of a variety of hormone receptors, including glucocorticoid receptor, mineralocorticoid receptor, androgen receptor, progesterone receptor, estrogen receptor, retinoic acid receptor, thyroid hormone receptor and vitamin D receptor. Proteins which bind to this sequence may **inhibit** hormone receptor induced gene transcription. Proteins which include this sequence may promote hormone

receptor induced gene transcription. The invention includes isolated DNA mols. for these proteins, methods of **treating** diseases using these proteins, synthetic peptides or their mimetics.

L4 ANSWER 28 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:11304 HCAPLUS
DOCUMENT NUMBER: 130:177891
TITLE: Vasostatin, a **calreticulin** fragment, **inhibits angiogenesis** and suppresses **tumor growth**
AUTHOR(S): Pike, Sandra E.; Yao, Lei; Jones, Karen D.; Cherney, Barry; Appella, Ettore; Sakaguchi, Kazuyasu; Nakhasi, Hira; Teruya-Feldstein, Julie; Wirth, Peter; Gupta, Ghanshyam; Tosato, Giovanna
CORPORATE SOURCE: Center for Biologics Evaluation and Research, Rockville, MD, 20852, USA
SOURCE: J. Exp. Med. (1998), 188(12), 2349-2356
CODEN: JEMEAV; ISSN: 0022-1007
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An **endothelial** cell **inhibitor** was purified from supernatant of an Epstein-Barr virus-immortalized cell line and identified as fragments of **calreticulin**. The purified recombinant NH2-terminal domain of **calreticulin** (amino acids 1-180) **inhibited** the proliferation of **endothelial** cells, but not cells of other lineages, and suppressed **angiogenesis** in vivo. We have named this NH2-terminal domain of **calreticulin** vasostatin. When inoculated into athymic mice, vasostatin significantly reduced **growth** of human Burkitt **lymphoma** and human colon **carcinoma**. Compared with other **inhibitors** of **angiogenesis**, vasostatin is a small, sol., and stable mol. that is easy to produce and deliver. As an **angiogenesis inhibitor** that specifically targets proliferating **endothelial** cells, vasostatin has a unique potential for **cancer treatment**.
REFERENCE COUNT: 46
REFERENCE(S): (1) Angiolillo, A; J Exp Med 1995, V182, P155 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 29 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:812027 HCAPLUS
DOCUMENT NUMBER: 130:166966
TITLE: The first subcomponent of complement, C1q, triggers the production of IL-8, IL-6, and monocyte chemoattractant peptide-1 by human umbilical vein endothelial cells
AUTHOR(S): Van den Berg, Rocco H.; Faber-Krol, Maria C.; Sim, Robert B.; Daha, Mohamed R.
CORPORATE SOURCE: Dep. Nephrol., Leiden Univ. Hosp., Leiden, Neth.

SOURCE: J. Immunol. (1998), 161(12), 6924-6930
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We and others have demonstrated previously the occurrence of cC1qR/CaR, a receptor for the collagen-like stalks of complement component C1q, on **endothelial** cells. In the present study we investigated whether binding of C1q to **endothelial** cells resulted in enhancement of cytokine or chemokine prodn. HUVEC produced 82.+-.91 pg/mL of IL-8, 79.+-.113 pg/mL of IL-6, and 503.+-.221 pg/mL of monocyte chemoattractant peptide-1 (MCP-1) under basal conditions. Incubation with C1q resulted in a time- and dose-dependent on de novo protein synthesis, as demonstrated by the detection of specific mRNA after C1q stimulation, and **inhibition** of peptide prodn. in the presence of cycloheximide. The prodn. of all factors was **inhibited** (69.+-.7%) by the collagenous fragments of C1q, while the C1q globular heads only induced 13.+-.11% **inhibition**. When HUVEC were incubated with C1q in the presence of aggregated IgM, enhanced prodn. of IL-8 (2500.+-.422 pg/mL), IL-6 (997.+-. 21 pg/mL), and MCP-1 (5343.+-.302 pg/mL) was found. Furthermore, F(ab')2 anti-**calreticulin** partially **inhibited** the prodn. of IL-8, confirming at least the involvement of cC1qR/CaR. These expts. suggest that in an inflammatory response C1q not only is able to activate the complement pathway, but when presented in a proper fashion also might induce the prodn. of factors that contribute to acute phase responses and recruitment of inflammatory cells.

REFERENCE COUNT: 32
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 30 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:640363 HCAPLUS
DOCUMENT NUMBER: 129:258972
TITLE: Identification of **tumor**-associated alleles of genes essential for cell viability and **growth** and the development of **neoplasm** **inhibitors** targetted against them
INVENTOR(S): Housman, David; Ledley, Fred D.; Stanton, Vincent P., Jr.
PATENT ASSIGNEE(S): Variagenics, Inc., USA
SOURCE: PCT Int. Appl., 605 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9841648 A2 19980924 WO 1998-US5419 19980319
WO 9841648 A3 19990429
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
AU 9867643 A1 19981012 AU 1998-67643 19980319
EP 973935 A2 20000126 EP 1998-912974 19980319
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRIORITY APPLN. INFO.: US 1997-41057 19970320
WO 1998-US5419 19980319

AB Strategies for the identification and targeting of specific alleles of genes in the **treatment** of **tumors** are described. **Tumor**-assocd. alleles of genes coding for proteins essential for cell viability or cell **growth** and that show loss of an alleles in **cancer** cells due to loss of heterozygosity (LOH) are identified. **Inhibitors** of the remaining allele, such as antisense nucleic acids or ribozymes, can then be developed. The method can also be used to **inhibit** the expression of particular alleles of genes for antigens in the control of transplant rejection. Particular categories of appropriate target genes are described, along with specific exemplary genes within those categories and methods of using such target genes. Antisense phosphorothioate oligonucleotides targeting RNA polymerase II and glutamyl/prolyl tRNA synthetase genes were tested for cytotoxicity in vitro. Oligonucleotides with a single base mismatch were significantly less toxic than those without mismatches. A no. of genes essential for proliferation were mapped and shown to be affected by loss-of-heterozygosity in oncogenesis.

L4 ANSWER 31 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:568937 HCAPLUS
DOCUMENT NUMBER: 129:200685
TITLE: Increasing plant growth rates by increasing the rate of the dark reaction of photosynthesis
INVENTOR(S): Basel, Richard M.; Elion, Glenn R.
PATENT ASSIGNEE(S): Agricola Technologies, Inc., USA
SOURCE: PCT Int. Appl., 143 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9836084	A2	19980820	WO 1998-US2501	19980206
WO 9836084	A3	19981217		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,

UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9861529 A1 19980908 AU 1998-61529 19980206
PRIORITY APPLN. INFO.: US 1997-801120 19970214
WO 1998-US2501 19980206

AB Methods of increasing rates of plant **growth** by **preventing** the dark reaction of photosynthesis from being rate limiting are described. This is achieved by increasing the efficiency of uptake and transport of carbon dioxide as carbonate using an animal carbonic anhydrase or by ensuring adequate pools of cofactors or other metabolites. Metal ion cofactors, such as Ca2+ and Zn2+, can be stored as complexes with metal binding proteins and phosphate can be stored in biomineralization proteins. The genes may be of microbial, plant or animal (specifically mammalian) origin. Tobacco plants transformed with a human carbonic anhydrase II gene under control of a 35S promoter showed faster **growth** than control plants. Similar, although less marked, effects were seen with genes for calcium-binding or hydroxyapatite-nucleating proteins. The effects of the genes were synergistic with the calcium-binding proteins also increasing plant calcium content approx. 10-fold without calcium supplementation of **growth** media. Expression of a metallothionein expression construct into potato increased **growth** rates and also plant resistance to cadmium.

L4 ANSWER 32 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:471187 HCAPLUS
DOCUMENT NUMBER: 129:228672
TITLE: Placental 57-kDa Ca2+-binding protein: regulation of expression and function in trophoblast calcium transport
AUTHOR(S): Hershberger, Marcia E.; Tuan, Rocky S.
CORPORATE SOURCE: Department of Orthopaedic Surgery, Thomas Jefferson University, Philadelphia, PA, 19107, USA
SOURCE: Dev. Biol. (1998), 199(1), 80-92
CODEN: DEBIAO; ISSN: 0012-1606
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB During gestation, transport by placental trophoblasts is solely responsible for nutrient supply to the developing fetus. The calcium (Ca) transport machinery of the placenta thus represents the primary tissue site for regulating fetal Ca homeostasis. The exact mechanism of trophoblast Ca transport is not known. However, there is evidence suggesting that a developmentally expressed cytosolic, trophoblast-specific, high Mr 57-kDa Ca-binding protein (CaBP) plays an important role in regulating and/or shuttling cytosolic Ca. The authors report the cloning of a full-length cDNA of the mouse CaBP which shows significant homol. with **calreticulin**, an endoplasmic reticulum-assocd. Ca binding protein. The functional role of CaBP in cellular Ca handling was investigated using a trophoblastic cell line, Rcho-1, derived from a rat **choriocarcinoma**. Upon differentiation, Rcho-1 cells exhibit enhanced Ca uptake compared to

undifferentiated Rcho-1 stem cells, and CaBP expression is upregulated. To analyze the regulation of CaBP expression, placenta organ cultures and Rcho-1 cells were **treated** for 48 h in vitro with a series of agents implicated in Ca homeostasis. In both placenta organ cultures and undifferentiated as well as differentiated Rcho-1 cells, **treatment** with 1,25-dihydroxy vitamin D3, estrogen, parathyroid hormone (PTH), parathyroid hormone-related protein (PTHrP 1-34), and Ca had no effect on CaBP mRNA and protein levels, which were significantly stimulated by PTHrP 67-84. PTHrP 67-84-**treated** Rcho-1 cells also exhibited higher Ca uptake activity than untreated control cells. The upregulation of CaBP expression during and/or following the differentiation of Rcho-1 cells into trophoblastic giant cells supports the importance of CaBP in trophoblast maturation and the validity of the Rcho-1 rat model cell system. In addn., the action of PTHrP on placental trophoblast Ca transport is likely to involve the regulation of CaBP expression to handle the increasing Ca requirements of the developing fetus. (c) 1998 Academic Press.

L4 ANSWER 33 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:285023 HCAPLUS
DOCUMENT NUMBER: 129:49886
TITLE: Folding of insulin receptor monomers is facilitated by the molecular chaperones calnexin and **calreticulin** and impaired by rapid dimerization
AUTHOR(S): Bass, Joseph; Chiu, Gavin; Argon, Yair; Steiner, Donald F.
CORPORATE SOURCE: The Department of Medicine, The University of Chicago, Chicago, IL, 60637, USA
SOURCE: J. Cell Biol. (1998), 141(3), 637-646
CODEN: JCLBA3; ISSN: 0021-9525
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Many complex membrane proteins undergo subunit folding and assembly in the ER before transport to the cell surface. Receptors for insulin and insulin-like **growth** factor I, both integral membrane proteins and members of the family of receptor tyrosine kinases (RTKs), are unusual in that they require homodimerization before export from the ER. To better understand chaperone mechanisms in endogenous membrane protein assembly in living cells, the authors have examd. the folding, assembly, and transport of the human insulin receptor (HIR), a dimeric RTK. Using pulse-chase labeling and nonreducing SDS-PAGE anal., the authors have explored the mol. basis of several sequential maturation steps during receptor biosynthesis. Under normal **growth** conditions, newly synthesized receptor monomers undergo disulfide bond formation while assocd. with the homologous chaperones calnexin (Cnx) and **calreticulin** (Crt). An **inhibitor** of glucose trimming, castanospermine (CST), abolished binding to Cnx/Crt but also unexpectedly accelerated receptor homodimerization resulting in misfolded oligomeric proreceptors whose processing was delayed and cell surface expression was also decreased by .apprx.30%. Prematurely-dimerized receptors were retained in the ER and more avidly assocd. with the heat shock protein of 70 kDa homolog binding protein. In CST-**treated** cells, receptor

misfolding followed disordered oligomerization. Together, these studies demonstrate a chaperone function for Cnx/Crt in HIR folding in vivo and also provide evidence that folding efficiency and homodimerization are counter-balanced.

L4 ANSWER 34 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:192728 HCAPLUS
DOCUMENT NUMBER: 128:292412
TITLE: Standardized characterization of gene expression in human colorectal epithelium by two-dimensional electrophoresis
AUTHOR(S): Reymond, Marc A.; Sanchez, Jean Charles; Hughes, Graham J.; Guenther, Klaus; Riese, Jutta; Tortola, Silvia; Peinado, Miguel A.; Kirchner, Thomas; Hohenberger, Werner; Hochstrasser, Denis F.; Koeckerling, Ferdinand
CORPORATE SOURCE: Dep. Surgery Pathology, Univ. Erlangen, Erlangen, D-91023, Germany
SOURCE: Electrophoresis (1997), 18(15), 2842-2848
CODEN: ELCTDN; ISSN: 0173-0835
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB New diagnostic and prognostic markers are needed in colorectal **cancer**. They can be found by differential anal. at DNA, RNA, or protein level. The accuracy of phenotypic comparisons of **tumor** and normal tissues depends on the purity of the samples. An effective method is presented to identify and isolate proteins that are differentially expressed under altered conditions, and a two-dimensional ref. protein map of the normal human colonic epithelium. Normal colonic mucosa, primary **tumors**, and liver metastases were prepd. in the operating room. After washing in an ice-cold medium contg. protease **inhibitors**, crypts were isolated by mech. prepn. without using metalloproteinases. Epithelial cells were then selected using Ber-EP4 Dynabeads. The samples were denaturated before processing for immobilized pH gradient two-dimensional polyacrylamide gel electrophoresis according to SWISS-2DPAGE stds. The samples contained more than 95% epithelial cells as confirmed by fluorescence-activated cell sorting using pan-anticytokeratin antibodies. Cell surfaces were not damaged, as assessed by scanning electronic microscope. A protein ref. map of the normal colonic epithelium was defined. Using gel matching, N-terminal sequencing and/or immunoblotting techniques, 60 polypeptides - including proteins specifically expressed in colorectal epithelium - have now been identified. This reproducible method of sample prepn. permits the comparison of protein patterns found in various pathol. states with the present ref. map (http://www.expasy.ch). Some of these patterns might provide diagnostic or prognostic markers, or even mol. targets for therapy in the future.

L4 ANSWER 35 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:192727 HCAPLUS
DOCUMENT NUMBER: 128:203697
TITLE: Protein expression profiles in human breast ductal carcinoma and histologically normal tissue

AUTHOR(S): Bini, Luca; Magi, Barbara; Marzocchi, Barbara; Arcuri, Felice; Tripodi, Sergio; Cintorino, Marcella; Sanchez, Jean Charles; Frutiger, Severine; Hughes, Graham; Pallini, Vitaliano; Hochstrasser, Denis F.; Tosi, Piero
CORPORATE SOURCE: Dep. Molecular Biology, Univ. Siena, Siena, I-53100, Italy
SOURCE: Electrophoresis (1997), 18(15), 2832-2841
CODEN: ELCTDN; ISSN: 0173-0835
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ref. two-dimensional (2-D) gels are presented for human breast ductal **carcinoma** and histol. normal tissue. Whole biopsy fragments were analyzed, including epithelial and nonepithelial components. Thirty-five spots have been assigned by gel matching to the human liver SWISS-2DPAGE ref. map and/or to the human primary keratinocyte IPG map from the Danish Center for Human Genome. N-terminal microsequencing was applied to confirm randomly chosen matching assignments and to identify 6 new spots. Protein expression profiles in ductal **carcinoma** and in normal breast tissue appeared to be similar, except for a pattern consisting of 32 spots, which were highly expressed in all **carcinoma** specimens, and less intense and occasionally undetectable in normal tissue. This difference was statistically significant. Assignment has been obtained for several spots, namely GRP94, GRP78, GRP75, mitochondrial HSP60, **calreticulin**, protein disulfide isomerase, peptidyl-prolyl cis-trans isomerase, collagen-binding protein 2, fructose bisphosphate aldolase, glyceraldehyde-3-phosphate dehydrogenase, thioredoxin, cytochrome c oxidase VA subunit, tubulin .beta. isoform, and macrophage migration **inhibitory** factor (MIF). The **cancer**- and tissue-specificity of the described pattern was assessed by matching to the Swiss-2DPAGE human liver, hepatoma, **lymphoma**, erythroleukemia ref. maps. The pattern of 32 spots was found to be indicative of epithelial neoplasia.

L4 ANSWER 36 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:138187 HCAPLUS
DOCUMENT NUMBER: 128:267996
TITLE: Genetic tailoring of N-linked oligosaccharides: the role of glucose residues in glycoprotein processing of Saccharomyces cerevisiae in vivo
AUTHOR(S): Jakob, Claude A.; Burda, Patricie; Te Heesen, Stephan; Aebi, Markus; Roth, Jurgen
CORPORATE SOURCE: Division of Cell and Molecular Pathology, Zurich, CH-8091, Switz.
SOURCE: Glycobiology (1998), 8(2), 155-164
CODEN: GLYCE3; ISSN: 0959-6658
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In higher eukaryotes a quality control system monitoring the folding state of glycoproteins is located in the ER and is composed of the proteins calnexin, **calreticulin**, glucosidase II, and UDP-glucose:glycoprotein glucosyltransferase. It is believed that the

innermost glucose residue of the N-linked oligosaccharide of a glycoprotein serves as a tag in this control system and therefore performs an important function in the protein folding pathway. To address this function, we constructed Saccharomyces cerevisiae strains which contain non-glucosylated (G0), monoglucosylated (G1), or diglucosylated (G2) glycoproteins in the ER and used these strains to study the role of glucose residues in the ER processing of glycoproteins. These alterations of the oligosaccharide structure did not result in a **growth** phenotype, but the induction of the unfolded protein response upon **treatment** with DTT was much higher in G0 and G2 strains as compared to wild-type and G1 strains. Our results provide in vivo evidence that the G1 oligosaccharide is an active oligosaccharide structure in the ER glycoprotein processing pathway of S. cerevisiae. Furthermore, by analyzing N-linked oligosaccharides of the constructed strains we can directly show that no general glycoprotein glucosyltransferase exists in S. cerevisiae.

L4 ANSWER 37 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:85569 HCAPLUS
DOCUMENT NUMBER: 128:202851
TITLE: Cell wall 1,6-.beta.-glucan synthesis in Saccharomyces cerevisiae depends on ER glucosidases I and II, and the molecular chaperone BiP/Kar2p
AUTHOR(S): Simons, Jan Fredrik; Ebersold, Melanie; Helenius, Ari
CORPORATE SOURCE: Department of Cell Biology, Yale University School of Medicine, New Haven, CT, 06520-8002, USA
SOURCE: EMBO J. (1998), 17(2), 396-405
CODEN: EMJODG; ISSN: 0261-4189
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of glucose trimming in the endoplasmic reticulum of Saccharomyces cerevisiae was investigated using glucosidase **inhibitors** and mutant strains devoid of glucosidases I and II. These glucosidases are responsible for removing glucose residues from the N-linked core oligosaccharides attached to newly synthesized polypeptide chains. In mammalian cells they participate together with calnexin, **calreticulin** and UDP-glucose:glycoprotein glucosyltransferase in the folding and quality control of newly synthesized glycoproteins. In S. cerevisiae, glucosidase II is encoded by the GLS2 gene, and glucosidase I, as suggested here, by the CWH41 gene. Using castanospermine (an .alpha.-glucosidase **inhibitor**) and yeast strains defective in glucosidase I, glucosidase II and BiP/Kar2p, it was demonstrated that cell wall synthesis depends on the two glucosidases and BiP/Kar2p. In double mutants with defects in both BiP/Kar2p and either of the glucosidases, the phenotype was particularly clear. Synthesis of 1,6-.beta.-glucan--a cell wall component-was reduced; the cell wall displayed abnormal morphol.; the cells aggregated; and their **growth** was severely **inhibited**. No defects in protein folding or secretion could be detected. It is concluded that glucose trimming in S. cerevisiae is necessary for proper cell wall synthesis, and that the glucosidases function synergistically with BiP/Kar2p in this process.

L4 ANSWER 38 OF 51 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:49834 HCAPLUS
DOCUMENT NUMBER: 126:127307
TITLE: Modulation of the retinoic acid and retinoid X receptor signaling pathways in P19 embryonal carcinoma cells by **calreticulin**
AUTHOR(S): Shago, Mary; Flock, Grace; Leung Hagesteijn, Chung-Yee; Woodside, Michael; Grinstein, Sergio; Giguere, Vincent; Dedhar, Shoukat
CORPORATE SOURCE: Mol. Oncol. Group, Royal Hospital, Montreal, PQ, H3A 1A1, Can.
SOURCE: Exp. Cell Res. (1997), 230(1), 50-60
CODEN: ECREAL; ISSN: 0014-4827
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Calreticulin** is a widely expressed calcium binding protein that can be bind to an amino acid sequence motif, KXGFFKR, which is present in the cytoplasmic domain of all integrin .alpha.-subunits. Closely related sequences, KXFFKR and KXFFRR, are encoded in the DNA-binding domain of all members of the steroid/thyroid/retinoid receptor superfamily and it has recently been demonstrated that **calreticulin inhibits** their activity both in vitro and in vivo. Here we present novel evidence that **calreticulin** can interfere directly with the retinoic acid (RARs) and retinoid X (RXRs) receptor pathways. **Calreticulin** exhibits the ability to **inhibit** DNA-binding activity of both heterodimeric RAR/RXR and homodimeric RXR complexes in vitro. **Inhibition** of RXR binding to DNA is achieved with a concn. of **calreticulin** that is approx. fourfold lower than that required for **inhibition** of RAR/RXR binding to a cognate binding site. Copptn. expts. suggest a direct protein:protein interaction between **calreticulin** and retinoid receptors. Stable overexpression of **calreticulin** in P19 embryonal **carcinoma** cell significantly decreases the rapid activation of the endogenous RA-responsive RAR.beta. gene, abrogates the ability of endogenous RAR/RXR complexes to bind to DNA, and **inhibits** the emergence of the RA-induced differentiated phenotype. These data demonstrate that **calreticulin** can interfere with the two distinct retinoid signaling pathways through a mechanism likely involving direct protein:protein interactions and that disruption of the retinoid signal alters biol. process in vivo.

L4 ANSWER 39 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:48815 HCAPLUS
DOCUMENT NUMBER: 126:65443
TITLE: Method of inhibiting restenosis using **calreticulin**
INVENTOR(S): Michalak, Marek; Lucas, Alexandra
PATENT ASSIGNEE(S): University of Alberta, Can.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9636643	A1	19961121	WO 1996-IB471	19960517
W: AU, CA, JP, MX				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9655120	A1	19961129	AU 1996-55120	19960517
PRIORITY APPLN. INFO.:			US 1995-442844	19950517
			US 1996-649417	19960516
			WO 1996-IB471	19960517

AB This invention relates to **calreticulin**, segments and derivs. thereof and to therapeutic compns. contg. such products for **treating** restenosis. It relates also to methods of producing the products by chem. synthesis or employing recombinant techniques. The invention is also concerned with the use of the products for **treating** patients to **prevent** atherosclerosis development as well as recurrent plaque **growth**. A method of **treating** a patient to **inhibit** restenosis comprises administering to such patient in an amt. which is effective to **inhibit** restenosis a compd. selected from the group consisting of **calreticulin**; the C-domain of **calreticulin**; a C-domain contg. segment of **calreticulin**; and a polypeptide which contains from about 6 to 100 amino acid residues and is an addn., substitution or deletion analog of the C-domain of **calreticulin** having the same functional activity. In a specific embodiment, the polypeptide has the amino acid sequence KEEEEKKRKEEEEAEEDEEDKDDKEDEDEDEEDKDEEEEE.

IT **144713-90-6P, Calreticulin** (human)
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; method of inhibiting restenosis using **calreticulin**)

L4 ANSWER 40 OF 51 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:	1996:647919 HCAPLUS
DOCUMENT NUMBER:	125:294014
TITLE:	Identification by subtractive hybridization of a spectrum of novel and unexpected genes associated with in vitro differentiation of human cytotrophoblast cells
AUTHOR(S):	Morrish, D. W.; Linetsky, E.; Bhardwaj, D.; Li, H.; Dakour, J.; Marsh, R. G.; Paterson, M. C.; Godbout, R.
CORPORATE SOURCE:	Department Medicine, University Alberta, Edmonton, AB, T6G 2S2, Can.
SOURCE:	Placenta (1996), 17(7), 431-441 CODEN: PLACDF; ISSN: 0143-4004
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB We have previously demonstrated that epidermal **growth** factor (EGF), colony stimulating factor-1 (CSF-1), and granulocyte-monocyte colony stimulating factor (GMCSF) stimulate, while transforming **growth** factor .beta.1 (TGF.beta.1) **inhibits**, cytotrophoblast differentiation. To identify genes mediating EGF-induced differentiation, we constructed a subtracted cDNA library between

undifferentiated cytotrophoblast and differentiating cytotrophoblast. We identified six novel genes and four known syncytial products .alpha.-human chorionic gonadotrophin (.alpha.hCG) pregnancy-specific .beta.1-glycoprotein, 3.beta.-hydroxysteroid dehydrogenase, and plasminogen activator **inhibitor** type 1 whose mRNAs increased during differentiation. Ten other genes were identified whose mRNAs increased during differentiation. Five of these (keratin 19, **calreticulin**, heat shock protein 27, serum and glucocorticoid-regulated kinase and adrenomedullin) were not previously reported to be expressed in placenta. Five other genes known to be expressed in placenta were identified: keratin 8, fibronectin, mitochondrial ATP synthase, H19, and cytosolic copper-zinc superoxide dismutase (SOD-1). Several of these genes may have regulatory functions in trophoblast differentiation.

L4 ANSWER 41 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:592346 HCAPLUS
DOCUMENT NUMBER: 125:271704
TITLE: Geranylgeraniol causes a decrease in levels of **calreticulin** and tyrosine phosphorylation of a 36-kDa protein prior to the appearance of apoptotic features in HL-60 cells
AUTHOR(S): Nakajo, Shigeo; Okamoto, Mitsuru; Masuda, Yutaka; Sakai, Itaru; Ohsawa, Shigemitsu; Nakaya, Kazuyasu
CORPORATE SOURCE: Lab. Biological Chem., Sch. Pharmaceutical Sci., Showa Univ., Tokyo, 142, Japan
SOURCE: Biochem. Biophys. Res. Commun. (1996), 226(3), 741-745
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It was demonstrated recently that geranylgeraniol (GGO) has potent apoptosis-inducing activity in various lines of **tumor** cells, including HL-60 cells. In the present study, the authors found that GGO markedly **inhibited** the expression of a Ca2+-binding protein, **calreticulin**, prior to the induction of apoptosis in HL-60 cells. Furthermore, they also obsd. a significant decrease in the tyrosine phosphorylation of a 36-kDa protein that is a major tyrosine-phosphorylated protein in HL-60 cells. These findings suggested that decreases in levels of **calreticulin** and in the tyrosine phosphorylation of the 36-kDa protein might be assocd. with the induction of apoptosis by GGO in HL-60 cells.

L4 ANSWER 42 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:580376 HCAPLUS
DOCUMENT NUMBER: 125:204501
TITLE: Use of **calreticulin** in modulating hormone responsiveness and new pharmaceuticals for **treating cancer**, osteoporosis and chronic inflammatory disease
INVENTOR(S): Dedhar, Shoukat
PATENT ASSIGNEE(S): Can.
SOURCE: Can. Pat. Appl., 42 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2140814	AA	19960724	CA 1995-2140814	19950123

AB This invention relates to isolated and purified proteins, such as **calreticulin** and mimetics of **calreticulin**, for a novel use of modulating hormone responsiveness. These proteins are useful in gene therapy and in manufg. pharmaceuticals for **treating** a variety of diseases, including **cancer**, osteoporosis and chronic inflammatory disease. The proteins include or bind to an amino acid sequence KXFFYR, wherein X is either G, A or V and Y is either K or R. This sequence is present in the DNA-binding domain, and is crit. for the DNA binding activity, of a variety of hormone receptors, including glucocorticoid receptor, mineralocorticoid receptor, androgen receptor, progesterone receptor, estrogen receptor, retinoic acid receptor, thyroid hormone receptor and vitamin D receptor. Proteins which bind to this sequence may **inhibit** hormone receptor-induced gene transcription. Proteins which include this sequence may promote hormone receptor-induced gene transcription. The invention includes isolated DNA mols. for these proteins, methods of **treating** diseases using these proteins, synthetic peptides and their mimetics, and kits contg. these proteins, synthetic peptides or their mimetics. **Calreticulin** was found to be present in cell nuclei. Both in vitro and in vivo, **calreticulin inhibited** hormone receptor-hormone responsive element interaction and hormone-induced gene transcription while KXFFYR peptides antagonized this **inhibition**.

L4 ANSWER 43 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:569705 HCAPLUS
DOCUMENT NUMBER: 125:204500
TITLE: **Calreticulin, calreticulin** mimics, and peptide inhibitors of **calreticulin** as modulators of hormone responsiveness and pharmaceuticals
INVENTOR(S): Dedhar, Shoukat; St-Arnaud, Rene
PATENT ASSIGNEE(S): Can.
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9623001	A1	19960801	WO 1995-CA664	19951123

W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE,

IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 5854202	A	19981229	US 1995-377432	19950124
AU 9539203	A1	19960814	AU 1995-39203	19951123
EP 807121	A1	19971119	EP 1995-936911	19951123
R: DE, DK, ES, FR, GB, IT, NL				
JP 2000507801	T2	20000627	JP 1996-522508	19951123
AU 9945861	A1	19991028	AU 1999-45861	19990901

PRIORITY APPLN. INFO.: US 1995-377432 A2 19950124
AU 1995-39203 A3 19951123
WO 1995-CA664 W 19951123

AB This invention relates to isolated and purified proteins, such as **calreticulin** and mimetics and **inhibitors** of **calreticulin**, for use in modulating hormone responsiveness. These proteins are useful in gene therapy and in manufg. pharmaceuticals for **treating** a variety of diseases, including **cancer**, osteoporosis and chronic inflammatory disease. The proteins include or bind to an amino acid sequence KXFFYR (X = G, A, V; Y = K, R). This sequence is present in the DNA-binding domain, and is crit. for the DNA binding activity, of a variety of hormone receptors, including glucocorticoid receptor, mineralocorticoid receptor, androgen receptor, progesterone receptor, estrogen receptor, retinoic acid receptor, thyroid hormone receptor and vitamin D receptor. Proteins which bind to this sequence may **inhibit** hormone receptor-induced gene transcription. Proteins which include this sequence may promote hormone receptor-induced gene transcription. The invention includes isolated DNA mols. for these proteins, methods of **treating** diseases using these proteins, synthetic peptides and their mimetics, and kits contg. these proteins, synthetic peptides or their mimetics. **Calreticulin** was visualized in cell nuclei. Recombinant **calreticulin inhibited** binding of androgen receptor to its response element. Neuronal differentiation of P19EC cells was **inhibited** by increased levels of **calreticulin** but enhanced by decreased levels of **calreticulin**. **Calreticulin** overexpression in osteoblastic cell line MC3T3-E1 also **inhibited** vitamin D-induced stimulation of calcium incorporation into the extracellular matrix.

L4 ANSWER 44 OF 51 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:	1996:381588 HCAPLUS
DOCUMENT NUMBER:	125:110917
TITLE:	**Inhibition** of retinoic acid receptor function and retinoic acid-regulated gene expression in mouse **melanoma** cells by **calreticulin**. A potential pathway for cyclic AMP regulation of retinoid action
AUTHOR(S):	Desai, Dinakar; Michalak, Marek; Singh, Nishi K.; Niles, Richard M.
CORPORATE SOURCE:	Department Biochemistry Molecular Biology, Marshall University School Medicine, Huntington, WV, 25755, USA
SOURCE:	J. Biol. Chem. (1996), 271(25), 15153-15159 CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Calcium is a second messenger that controls a wide variety of cellular functions. Because of its multiple actions, there is a stringent requirement for calcium homeostasis, and this is achieved in part by a system of transport and storage proteins such as **calreticulin** located in the endoplasmic reticulum. **Calreticulin** is also found in the nucleus, suggesting that it may have a role in transcriptional regulation. It has been reported that **calreticulin** can **inhibit** steroid-regulated gene transcription by **preventing** receptor binding to DNA. Here we report that overexpression of the **calreticulin** gene in B16 mouse **melanoma** cells resulted in a decrease in retinoic acid (RA)-stimulated reporter gene expression. Gel shift anal. showed that purified **calreticulin inhibited** the binding of endogenous RAR to a .beta.-RA response element oligonucleotide, only if added prior the addn. of the oligonucleotide. Co-immunopptn. studies suggest a phys. interaction between RAR and **calreticulin**. Transfection of the **calreticulin** gene into B16 cells **inhibited** the RA induction of protein kinase C.alpha., a marker of RA-induced differentiation. We also found that cAMP increased the expression of **calreticulin**. CAMP may act to antagonize RA action by both decreasing RAR expression and stimulating **calreticulin** levels.

L4 ANSWER 45 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:245004 HCAPLUS
DOCUMENT NUMBER: 125:183
TITLE: Control of tumor progression by maintenance of apoptosis
AUTHOR(S): Bruchovsky, Nicholas; Snoek, Rob; Rennie, Paul S.; Akakura, Koichiro; Goldenberg, S. Larry; Gleave, Martin
CORPORATE SOURCE: Department Cancer Endocrinology, BC Cancer Agency, Vancouver, BC, V5Z 4E6, Can.
SOURCE: Prostate (N. Y.) (1996), (Suppl. 6), 13-21
CODEN: PRSTDS; ISSN: 0270-4137
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review, with 27 refs. The ability to induce multiple apoptotic regressions of an androgen-dependent **tumor** cell population by repeated cycles of androgen withdrawal and replacement may be advantageous in therapeutic strategies aimed at delaying or **preventing** **tumor** progression. With greater insight into factors that either initiate or limit apoptosis, more efficient application of intermittent therapy might be achieved, esp. if methods could be devised to increase the length or no. of **treatment** cycles. Both **calreticulin** and clusterin represent proteins with a potential role in the regulation of apoptosis. **Calreticulin** may **inhibit** target gene transcription by interacting with steroid hormone receptors, thereby masking their DNA-binding sites and triggering the onset of the apoptotic process. Clusterin, on the other hand, is a membrane-stabilizing protein that appears to be involved in limiting the autophagic lysis of epithelial cells during apoptosis. Also, the increasing tendency for nuclear localization of clusterin after androgen withdrawal may preserve the nuclear environment, limiting the lethal

effect of **treatment**. Thus, **tumor** progression, characterized by the loss of apoptotic potential, appears to be linked in part to the inappropriate activation of the TRPM-2 gene, which accounts for the constitutive expression of clusterin.

L4 ANSWER 46 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:175690 HCAPLUS
DOCUMENT NUMBER: 124:220506
TITLE: Inositol triphosphate receptors as targets for treating cell proliferative disorders by modulating signal transduction
INVENTOR(S): Fischer, Gabriela A.; Ullrich, Axel
PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V., Germany
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9600586	A2	19960111	WO 1995-EP2532	19950629
WO 9600586	A3	19960215		

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT

RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9529789	A1	19960125	AU 1995-29789	19950629

PRIORITY APPLN. INFO.: US 1994-268390 19940630
WO 1995-EP2532 19950629

AB The present invention relates to the use of proteins, peptides and org. mols. capable of modulating inositol 1,4,5-triphosphate (IP3) receptor signal transduction in order to **inhibit** or reverse inappropriate **growth** of cells assocd. with abnormalities of signal transduction assocd. with tyrosine kinases. The present invention also relates to the use of IP3 receptor mutants in the **treatment** of proliferative disorders assocd. with abnormalities of signal transduction assocd. with tyrosine kinases, including **cancer**. The present invention also relates to the use of IP3 receptor and genetically engineered host cells that express the IP3 receptor to evaluate and screen for substances and compds. that modulate IP3 receptor activities.

L4 ANSWER 47 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:796651 HCAPLUS
DOCUMENT NUMBER: 123:189325
TITLE: Components of the protein synthesis and folding machinery are induced in vascular smooth muscle cells by hypertrophic and hyperplastic agents. Identification by comparative protein phenotyping and

microsequencing
AUTHOR(S): Patton, Wayne F.; Erdjument-Bromage, Hediye; Marks, Andrew R.; Tempst, Paul; Taubman, Mark B.
CORPORATE SOURCE: Mol. Biol. Program, Memorial Sloan-Kettering Cancer Cent., New York, NY, 10021, USA
SOURCE: J. Biol. Chem. (1995), 270(36), 21404-10
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Vascular smooth muscle cells (VSMC) are the principal cellular component of the blood vessel wall. Atherosclerosis, hypertension, and **angiogenesis** are assocd. with abnormal VSMC **growth**. Angiotensin II is hypertrophic for cultured adult rat aortic VSMC, whereas platelet-derived **growth** factor and serum are hyperplastic. To identify changes in specific proteins assocd. with either hyperplastic or hypertrophic **growth**, high resoln. two-dimensional gel electrophoresis was performed on exts. from quiescent rat aortic VSMC and from VSMC exposed for 24 h to **growth** factors (10% fetal calf serum, platelet-derived **growth** factor, or angiotensin II). Twelve proteins were up-regulated and 5 down-regulated by **treatment** with **growth** factors. Eight of the up-regulated and one of the down-regulated proteins were identified by internal protein microsequencing from electroblotted two-dimensional gels or by co-electrophoresis of purified proteins in two-dimensional gels. Four of the proteins up-regulated by **growth** factors were identified as mediators of protein folding. These were heat shock proteins, HSP-60 and HSP-70, protein disulfide isomerase, and protein disulfide isomerase isoenzyme Q-2. Addnl. proteins were identified as elongation factor EF-1.beta., a component of the protein synthesis app., and **calreticulin**, another putative mol. chaperone. Vimentin and actin were also upregulated, whereas an isoform of myosin heavy chain was down-regulated. Hyperplastic and hypertrophic **growth** were accompanied by similar changes in protein expression, suggesting that both types of **growth** require up-regulation of the protein synthesis and folding machinery.

L4 ANSWER 48 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:688145 HCAPLUS
DOCUMENT NUMBER: 123:78641
TITLE: Enhanced expression of **calreticulin** in the nucleus of radioresistant squamous carcinoma cells in response to ionizing radiation
AUTHOR(S): Ramsamooj, Priya; Notario, Vicente; Dritschilo, Anatoly
CORPORATE SOURCE: Dep. of Radiation Medicine, Georgetown Univ. Med. Center, Washington, DC, 20007, USA
SOURCE: Cancer Res. (1995), 55(14), 3016-21
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ionizing radiation has been shown to modulate gene and protein expression as well as cellular signal transduction pathways. However, the biochem. and mol. mechanisms that underlie the cellular response to radiation are not fully understood. The effects of ionizing radiation on the expression

of nuclear proteins have now been investigated in radioresistant human head and neck squamous **carcinomas** cells (SQ-20B cells) using the techniques of two-dimensional PAGE, silver staining, and computer-assisted quant. anal. .gamma.-Radiation (600 cGy) induced the expression of 10 proteins and suppressed the expression of 5 proteins in the nuclei of SQ-20B cells as detected 4 h after **treatment**. Electroelution and NH2-terminal amino acid sequence anal. revealed that one of the radiation-induced proteins was the Ca2+-binding protein **calreticulin**. The expression of **calreticulin** was increased approx. 6-fold in the nuclei of irradiated SQ-20B cells. **Calreticulin** and the other proteins whose expression was affected by radiation may contribute to the radioresistance phenotype of SQ-20B cells.

L4 ANSWER 49 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:685391 HCAPLUS
DOCUMENT NUMBER: 123:140514
TITLE: Cell surface **calreticulin** is a putative mannoside lectin which triggers mouse melanoma cell spreading
AUTHOR(S): White, Tracy K.; Zhu, Qiang; Tanzer, Marvin L.
CORPORATE SOURCE: Dep. BioStructure and Function, Univ. Connecticut Health Center, Farmington, CT, 06030-3705, USA
SOURCE: J. Biol. Chem. (1995), 270(27), 15926-9
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB B16 mouse **melanoma** cells adhere to and spread on laminin. We have previously shown that cell preading is uncoupled from adhesion when unglycosylated laminin is used as a substratum; spreading was restored by a Pronase digest of laminin which became inactive when it was specifically depleted of its mannoside peptides; spreading was also specifically restored by mannosides such as mannan, Man9, and Man6, but not Man3. The effector mannosides bind to a cell surface receptor, previously shown by direct and indirect methods. We have now identified the receptor as cell surface **calreticulin** by isolating it via mannan affinity chromatog. and showing its sequence identity with mouse **calreticulin**. Anti-**calreticulin** antibodies confirm this identity, decorate the B16 cell surface, and block cell spreading. Purified B16 cell **calreticulin** from whole cell lysates successfully competes with cell surface **calreticulin** and **prevents** cell spreading. The composite data implicate cell surface **calreticulin** as a putative lectin that must be occupied to initiate spreading of laminin-adherent B16 cells.

L4 ANSWER 50 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:500297 HCAPLUS
DOCUMENT NUMBER: 122:255933
TITLE: **Calreticulin**, an antithrombotic agent which binds to vitamin K-dependent coagulation factors, stimulates endothelial nitric oxide production, and limits thrombosis in canine coronary arteries
AUTHOR(S): Kuwabara, Keisuke; Pinsky, David J.; Schmidt, Ann Marie; Benedict, Claude; Brett, Jerold; Ogawa,

Satoshi; Broekman, M. Johan; Marcus, Aaron J.; Sciacca, Robert R.; et al.
CORPORATE SOURCE: Coll. Physicians and Surgeons, Columbia Univ., New York, NY, 10032, USA
SOURCE: J. Biol. Chem. (1995), 270(14), 8179-87
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Coagulation Factor IX/IXa has been shown to bind to cellular surfaces, and Factor IXa expresses its procoagulant activity by assembling into the intrinsic Factor X activating complex (Factors IXa/VIIIa/X), which also forms on membrane surfaces. This led us to identify cellular proteins which bind Factor IX/IXa; an .apprxeq.55-kDa polypeptide was purified to homogeneity from bovine lung exts. based on its capacity to bind 125I-Factor IX in a dose-dependent and saturable manner. From protein sequence data of the amino terminus and internal peptides, the .apprxeq.55-kDa polypeptide was identified as **calreticulin**, a previously identified intracellular calcium-binding protein. Recombinant **calreticulin** bound vitamin K-dependent coagulation factors, 125I-Factor IX, 125I-Factor X, and 125I-prothrombin (Kd values of .apprxeq.2.7, 3.2, and 8.3 nM, resp.), via interaction with its C-domain, although it did not affect the coagulant properties of these proteins. 125I-**Calreticulin** also bound to **endothelial** cells in vitro (Kd .apprxeq. 7.4 nM), and mouse infusion studies showed an initial rapid phase of clearance in which **calreticulin** could be localized on the vascular **endothelium**. Exposure of **endothelial** cells to **calreticulin** led to dose-dependent, immediate, and sustained increase in the prodn. of nitric oxide, as measured using a porphyrinic microsensor. In a canine elec. induced thrombosis model, intracoronary infusion of **calreticulin** (n = 7) **prevented** occlusion of the left circumflex coronary artery in a dose-dependent manner compared with vehicle-**treated** controls (n = 5). These results indicate that **calreticulin** interacts with the **endothelium** to stimulate release of nitric oxide and **inhibit** clot formation.

L4 ANSWER 51 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:629264 HCAPLUS
DOCUMENT NUMBER: 115:229264
TITLE: Regulation of expression and intracellular distribution of **calreticulin**, a major calcium binding protein of nonmuscle cells
AUTHOR(S): Opas, Michal; Dziak, Ewa; Fliegel, Larry; Michalak, Marek
CORPORATE SOURCE: Dep.

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L1 41 SEA FILE=REGISTRY CALRETICULIN?/CN
L2 742 SEA FILE=HCAPLUS L1 OR ?CALRETICULIN?
L4 51 SEA FILE=HCAPLUS L2 AND (?CANCER? OR ?CARCIN? OR ?NEOPLASM? OR ?TUMOR? OR ?TUMOUR? OR ?SARCOM? OR ?LYMPHOM? OR MELANO? OR LEUKEM? OR ANGIOGEN? OR ENDOTHEL? OR GROWTH)(L)(INHIBIT? OR PREVENT? OR TREAT?)

=> d ibib abs hitrn l4 1-51

L4 ANSWER 1 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:656862 HCAPLUS
TITLE: Tumor-specific immunity and antiangiogenesis generated by a DNA vaccine encoding **calreticulin** linked to a tumor antigen
AUTHOR(S): Cheng, Wen-Fang; Hung, Chien-Fu; Chai, Chee-Yin; Hsu, Keng-Fu; He, Liangmei; Ling, Morris; Wu, T.-C.
CORPORATE SOURCE: Department of Pathology, Johns Hopkins Medical Institutions, Baltimore, MD, USA
SOURCE: J. Clin. Invest. (2001), 108(5), 669-678
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: American Society for Clinical Investigation
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Antigen-specific **cancer** immunotherapy and antiangiogenesis have emerged as two attractive strategies for **cancer treatment**. An innovative approach that combines both mechanisms will likely generate the most potent **antitumor** effect. We tested this approach using **calreticulin** (CRT), which has demonstrated the ability to enhance MHC class I presentation and exhibit an antiangiogenic effect. We explored the linkage of CRT to a model **tumor** antigen, human papilloma virus type-16 (HPV-16) E7, for the development of a DNA vaccine. We found that C57BL/6 mice vaccinated intradermally with CRT/E7 DNA exhibited a dramatic increase in E7-specific CD8+ T cell precursors and an impressive **antitumor** effect against E7-expressing **tumors** compared with mice vaccinated with wild-type E7 DNA or CRT DNA. Vaccination of CD4/CD8 double-depleted C57BL/6 mice and immunocompromised (BALB/c nu/nu) mice with CRT/E7 DNA or CRT DNA generated significant redn. of lung **tumor** nodules compared with wild-type E7 DNA, suggesting that antiangiogenesis may have contributed to the **antitumor** effect. Examn. of microvessel d. in lung **tumor** nodules and an in vivo **angiogenesis** assay further confirmed the antiangiogenic effect generated by CRT/E7 and CRT. Thus, **cancer** therapy using CRT linked to a **tumor** antigen holds promise for **treating tumors** by combining antigen-specific immunotherapy and antiangiogenesis.

REFERENCE COUNT: 54

REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 51 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:618207 HCAPLUS

DOCUMENT NUMBER: 135:190398

TITLE: Nucleic acid markers useful for the identification, assessment, **prevention** and therapy of human **cancers**

INVENTOR(S): Roth, Frederick P.; Van Huffel, Christophe; White, James V.; Shyjan, Andrew W.

PATENT ASSIGNEE(S): Millennium Predictive Medicine, Inc., USA

SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001061048	A2	20010823	WO 2001-US5263	20010216

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-183312 P 20000217

AB The present invention is directed to the identification of markers that can be used to det. the sensitivity of cancer cells to a therapeutic agent. The present invention is also directed to the identification of therapeutic targets. Nucleic acid arrays were used to det. the level of expression of sequences (genes) found in 60 different solid tumor cancer cell lines selected form the NCI 60 cancer cell line series. Expression anal. was used to identify markers assocd. with sensitivity to certain chemotherapeutic agents.

IT **144713-90-6, Calreticulin** (human clone Ro38-1 precursor protein moiety reduced)
RL: ANT (Analyte); BOC (Biological occurrence); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(amino acid sequence; nucleic acid markers useful for the identification, assessment, **prevention** and therapy of human **cancers**)

L4 ANSWER 3 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:545510 HCAPLUS
DOCUMENT NUMBER: 135:121187
TITLE: Compositions and methods using heat-shock protein-antigen complexes to treat neurodegenerative disorders, and isolation of the complexes
INVENTOR(S): Srivastava, Pramod K.
PATENT ASSIGNEE(S): University of Connecticut Health Center, USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001052877	A1	20010726	WO 2001-US1671	20010118

W: AU, CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

PRIORITY APPLN. INFO.: US 2000-489215 A 20000121

AB The invention provides compns. comprising complexes of heat-shock proteins noncovalently or covalently linked to antigens that display the antigenicity of antigens found in cells and tissues assocd. with the pathol. of a neurodegenerative disease or disorder (e.g. Alzheimer's Disease). The compns. may be isolated from any tissue sources in which they exist, e.g. diseased human cells, non-human models for the disease or, in vitro cultured cells that express neurodegenerative disorder-assocd. antigens. The invention further provides methods for the prevention and treatment of neurodegenerative diseases or disorders using

the compns. of the invention. The invention also provides kits comprising the compns. of the invention.

L4 ANSWER 4 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:545437 HCAPLUS
DOCUMENT NUMBER: 135:142201
TITLE: Complexes of peptide-binding fragments of heat shock proteins and their use as immunotherapeutic agents
INVENTOR(S): Srivastava, Pramod K.
PATENT ASSIGNEE(S): University of Connecticut Health Center, USA
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001052791	A2	20010726	WO 2001-US1781	20010118

W: AU, CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

PRIORITY APPLN. INFO.: US 2000-488393 A 20000120
AB The present invention relates to pharmaceutical compns. comprising peptide-binding fragments of heat shock proteins (HSPs) and noncovalent complexes of peptide-binding fragments of HSPs in noncovalent assocn. with antigenic mols. The invention further relates to methods for the use of such pharmaceutical compns. as immunotherapeutic agents for the **treatment** and **prevention** of infectious diseases and **cancer**.

L4 ANSWER 5 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:473659 HCAPLUS
DOCUMENT NUMBER: 135:205729
TITLE: Microarray analysis of the in vivo effects of hypophysectomy and **growth** hormone **treatment** on gene expression in the rat
AUTHOR(S): Flores-Morales, Amilcar; Stahlberg, Nina; Tollet-Egnell, Petra; Lundeberg, Joakim; Malek, Renae L.; Quackenbush, John; Lee, Norman H.; Norstedt, Gunnar
CORPORATE SOURCE: Department of Molecular Medicine, Karolinska Institute, Stockholm, 17176, Swed.
SOURCE: Endocrinology (2001), 142(7), 3163-3176
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors used cDNA microarrays contg. 3000 different rat genes to study the consequences of severe hormonal deficiency (hypophysectomy) on the gene expression patterns in heart, liver, and kidney. Hybridization signals were seen from a majority of the arrayed cDNAs; nonetheless, tissue-specific expression patterns could be delineated. Hypophysectomy

affected the expression of genes involved in a variety of cellular functions. Between 16-29% of the detected transcripts from each tissue changed expression level as a reaction to this condition. Chronic treatment of hypophysectomized animals with human GH also caused significant changes in gene expression patterns. The study confirms previous knowledge concerning certain gene expression changes in the above-mentioned situations and provides new information regarding hypophysectomy and chronic human GH effects in the rat. Furthermore, the authors have identified several new genes that respond to GH treatment. The results represent a first step toward a more global understanding of gene expression changes in states of hormonal deficiency.

REFERENCE COUNT: 92
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 51 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:456229 HCAPLUS
DOCUMENT NUMBER: 135:194164
TITLE: Mapping and expression pattern analysis of key components of the major histocompatibility complex class I antigen processing and presentation pathway in a representative human renal cell carcinoma cell line
AUTHOR(S): Lichtenfels, Rudolf; Ackermann, Angelika; Kellner, Roland; Seliger, Barbara
CORPORATE SOURCE: IIIrd Department of Internal Medicine, Johannes Gutenberg University, Mainz, D-55101, Germany
SOURCE: Electrophoresis (2001), 22(9), 1801-1809
CODEN: ELCTDN; ISSN: 0173-0835
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Renal cell **carcinoma** (RCC) represent approx. 5% of all **cancer** deaths. At the time of presentation, over 50% of the patients have already developed locally advanced or metastatic disease with five-year survival rates of less than 20%. Although relative resistant to conventional regimens, RCC are partially susceptible to T cell-based immunotherapy. To further develop this **treatment** modality, two-dimensional PAGE (2-D PAGE) was applied for both the mapping of the key components of the major histocompatibility complex (MHC) class I antigen processing and presentation machinery (APM) and the characterization of the constitutive and cytokine-regulated protein expression profiles in a representative human RCC cell line. The latter aspect is based on the fact, that the expression level of some of the APM components can be altered in response to interferon (IFN)-.gamma. **treatment**. Total cell lysates from untreated and IFN-.gamma.-**treated tumor** cells were sepd. on 2-D PAGE gels using broad range immobilized pH gradient (IPG) strips. Serial Western blot

analyses using sets of APM-specific antibodies were performed to target the relevant protein spots. Protein verification was mostly accomplished via peptide mass finger-printing using matrix-assisted laser desorption/ionization-mass spectrometry (MALDI-MS). To date, the majority of the APM-related components have been identified and mapped. In addn., the different protein expression profiles of untreated and IFN-.gamma.-**treated** RCC cells are under investigation.

REFERENCE COUNT: 36

REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:380422 HCAPLUS
DOCUMENT NUMBER: 134:365715
TITLE: Cytokine compositions for modulating ER stress-induced cholesterol/triglyceride accumulation
INVENTOR(S): Austin, Richard C.; Werstuck, Geoff
PATENT ASSIGNEE(S): Hamilton Civic Hospitals Research Centre Inc., Can.
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001035986	A2	20010525	WO 2000-CA1372	20001116

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-166114 P 19991116

AB The present invention provides methods for **preventing** the accumulation of cholesterol/triglycerides within mammalian cells. The present methods are based upon the surprising discovery that endoplasmic reticulum (ER) stress in a cell, e.g., **endothelial** cells, smooth muscle, macrophages, and hepatic cells, leads to cholesterol/triglyceride accumulation within the cell, which cholesterol/triglyceride accumulation is often a causative factor in the development of any of a no. of conditions or diseases, such as atherosclerosis. The ER stress can be the result of any of a variety of causes, including homocysteine, viral infection, and hypoxia. Accordingly, counteracting the progression or the severity of ER stress by a cytokine, e.g., interleukin-3, can be used to

inhibit the accumulation of cholesterol/triglycerides in said cell, thereby **preventing** or lessening the severity of any of a no. of cholesterol-related diseases or conditions, e.g., atherosclerosis. In addn., the presence of ER stress in a cell can be used to diagnose a cholesterol assocd. disease, or to predict the propensity of a mammal to develop a disease.

L4 ANSWER 8 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:338762 HCAPLUS
DOCUMENT NUMBER: 134:362292
TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
INVENTOR(S): Farr, Spencer
PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165398 P 19991105
US 2000-196571 P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to det. the hypersensitivity of individuals to a given agent, such as drug or other chem., in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes assocd. with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes assocd. with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes assocd. with hypersensitivity. The expression of the genes predetd. to be assocd. with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and app. useful for identifying hypersensitivity in a subject are also disclosed.

L4 ANSWER 9 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:230502 HCAPLUS
DOCUMENT NUMBER: 134:365952
TITLE: IgA cross-reactivity between a nuclear autoantigen and wheat proteins suggests molecular mimicry as a possible pathomechanism in celiac disease
AUTHOR(S): Natter, Susanne; Granditsch, Gerhard; Reichel, Gerlinde L.; Baghestanian, Mehrdad; Valent, Peter; Elfman, Lena; Gronlund, Hans; Kraft, Dietrich; Valenta, Rudolf
CORPORATE SOURCE: Department of Pathophysiology, AKH, University of Vienna, Vienna, Austria
SOURCE: Eur. J. Immunol. (2001), 31(3), 918-928
CODEN: EJIMAF; ISSN: 0014-2980
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Celiac disease patients display IgA antibody reactivity to wheat as well as to human proteins. We used serum IgA from celiac patients and, for control purposes, from patients with Crohn's disease, ulcerative colitis and from healthy individuals to identify celiac disease-specific IgA autoantigens in nitrocellulose-blotted exts. from various human cell types (epithelial, **endothelial**, intestinal cells, fibroblasts). The pattern, recognition intensity and time course of IgA autoreactivity was monitored using serial serum samples obtained from celiac children before and under gluten-free diet. By immunoblot **inhibition** and subcellular (cytosolic, nuclear) cell fractionation we identified a 55 kDa nuclear autoantigen expressed in intestinal, **endothelial** cells and in fibroblasts which was recognized by IgA antibodies of approx. half of the celiac disease patients and cross-reacted with wheat proteins. IgA reactivity to the 55 kDa autoantigen disappeared during gluten-free diet and was **inhibited** after pre-absorption of sera with wheat proteins but not with tissue transglutaminase, previously reported as the unique celiac disease-specific autoantigen. In conclusion, we defined a novel 55 kDa celiac disease-specific nuclear IgA autoantigen which shares epitopes with wheat proteins and which is different from tissue transglutaminase and **calreticulin**. Although the newly defined autoantigen was recognized much less frequently than tissue transglutaminase, our data suggest mol. mimicry between wheat and human proteins as a possible pathomechanism for the induction and/or maintenance of mucosal tissue damage in celiac disease.

REFERENCE COUNT: 44
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:150908 HCAPLUS

DOCUMENT NUMBER: 134:309402
TITLE: Characterization of the major histocompatibility complex class I deficiencies in B16 melanoma cells
AUTHOR(S): Seliger, Barbara; Wollscheid, Ursula; Momburg, Frank; Blankenstein, Thomas; Huber, Christoph
CORPORATE SOURCE: Johannes Gutenberg Universitat, III. Medizinische Klinik, Mainz, 55131, Germany
SOURCE: Cancer Res. (2001), 61(3), 1095-1099
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The murine B16 **melanoma** system represents an important in vivo model for the evaluation of T cell-based immunization and vaccination strategies, although deficient MHC class I surface expression has been identified in these cells. The authors postulate here that the MHC class I-deficient phenotype of B16 **melanoma** cells is attributable to down-regulation or the loss of the expression and function of multiple components of the MHC class I antigen-processing pathway, including the peptide transporter assocd. with antigen processing, the proteasome subunits LMP2, LMP7, and LMP10, PA28.alpha. and -.beta., and the chaperone tapasin. In contrast, calnexin, **calreticulin**, ER60, and protein disulfide isomerase expression are unaltered or only marginally suppressed in these cells. The level of down-regulation of the components of the antigen-processing pathway is either transcriptionally or post-transcriptionally controlled and could be cor. in all cases by IFN-.gamma. **treatment**, which also reconstituted MHC class I surface expression. Thus, B16 **melanoma** cells can be used as a model for the characterization of the mechanisms underlying the coordinated dysregulation of the antigen-processing components, which should provide new insights into the development of **tumors** and the factors controlling this process.

REFERENCE COUNT: 38
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:105937 HCAPLUS
DOCUMENT NUMBER: 134:158091
TITLE: Activation of extracellular signal-regulated kinases (ERKs) defines the first phase of 1,25-dihydroxyvitamin D3-induced differentiation of HL60 cells
AUTHOR(S): Wang, Xuening; Studzinski, George P.
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, UMDNJ-New Jersey Medical School, Newark, NJ, 07103, USA
SOURCE: J. Cell. Biochem. (2000), 80(4), 471-482
CODEN: JCEBD5; ISSN: 0730-2312

PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Activation of ERK1 and ERK2 protein kinases has been implicated in diverse cellular processes, including the control of cell proliferation and cell differentiation. In human myeloblastoid **leukemia** HL60 cells rapid (.apprx.15 min) but transient activation of ERK1/2 has been reported following induction of macrophage/monocyte differentiation by phorbol esters, or by very high (10-6 M) concns. of 1,25-dihydroxyvitamin D3 (1,25D3), while retinoic acid-induced granulocytic differentiation was accompanied by sustained activation of ERK1/2. The authors report that monocytic differentiation of HL60 cells induced by moderate (10-9 to 10-7 M) concns. of 1,25D3 could be divided into at least two stages. In the first phase, which lasts 24-48h, the cells continued in the normal cell cycle while expressing markers of monocytic phenotype, such as CD14. In the next phase the onset of G1 cell cycle block became apparent and expression of CD11b was prominent, indicating a more mature myeloid phenotype. The first phase was characterized by high levels of ERKs activated by phosphorylation, and these decreased as the cells entered the second phase, while the levels of p27/Kip1 increased at that time. Serum-starved or PD98059-**treated** HL60 cells had reduced **growth** rate and slower differentiation, but the G1 block also coincided with decreased levels of activated ERK1/2. The data suggest that the MEK/ERK pathway maintains cell proliferation during 1,25D3-induced monocytic differentiation of HL60 cells, but that ERK1/2 activity becomes suppressed during the later stages of differentiation, and the consequent G1 block leads to "terminal" differentiation.

REFERENCE COUNT: 42
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:831887 HCAPLUS
DOCUMENT NUMBER: 134:111402
TITLE: Aluminum-induced 1.fwdarw.3-.beta.-D-glucan inhibits cell-to-cell trafficking of molecules through plasmodesmata. A new mechanism of aluminum toxicity in plants
AUTHOR(S): Sivaguru, Mayandi; Fujiwara, Toru; Samaj, Josef; Baluska, Frantisek; Yang, Zhenming; Osawa, Hiroki; Maeda, Takanori; Mori, Tomoko; Volkmann, Dieter; Matsumoto, Hideaki
CORPORATE SOURCE: Research Institute for Bioresources, Okayama University, Kurashiki, 710-0046, Japan
SOURCE: Plant Physiol. (2000), 124(3), 991-1005
CODEN: PLPHAY; ISSN: 0032-0889
PUBLISHER: American Society of Plant Physiologists
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Symplastic intercellular transport in plants is achieved by plasmodesmata (PD). These cytoplasmic channels are well known to interconnect plant cells to facilitate intercellular movement of water, nutrients, and signaling mols. including hormones. However, it is not known whether Al may affect this cell-to-cell transport process, which is a crit. feature for roots as organs of nutrient/water uptake. The authors have microinjected the dye lucifer yellow carbohydrazide into peripheral root cells of an Al-sensitive wheat (Triticum aestivum cv Scout 66) either before or after Al **treatment** and followed the cell-to-cell dye-coupling through PD. Here, the authors show that the Al-induced root **growth inhibition** is closely assocd. with the Al-induced blockage of cell-to-cell dye coupling. Immunofluorescence combined with immuno-electron microscopic techniques using monoclonal antibodies against 1.fwdarw.3-.beta.-D-glucan (callose) revealed circumstantial evidence that Al-induced callose deposition at PD may be responsible for this blockage of symplastic transport. Use of 2-deoxy-D-glucose, a callose synthesis **inhibitor**, allowed the authors to demonstrate that a redn. in callose particles correlated well with the improved dye-coupling and reduced root **growth inhibition**. While assessing the tissue specificity of this Al effect, comparable responses were obtained from the dye-coupling pattern in tobacco (Nicotiana tabacum) mesophyll cells. Analyses of the Al-induced expression of PD-assocd. proteins, such as **calreticulin** and unconventional myosin VIII, showed enhanced fluorescence and co-localizations with callose deposits. These results suggest that Al signal-mediated localized alterations to calcium homeostasis may drive callose formation and PD closure. Thus, extracellular Al-induced callose deposition at PD could effectively block symplastic transport and communication in higher plants.

REFERENCE COUNT: 75

REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:820413 HCAPLUS
DOCUMENT NUMBER: 134:365408
TITLE: Coordinate downregulation of multiple MHC class I antigen processing genes in chemical-induced murine tumor cell lines of distinct origin
AUTHOR(S): Seliger, B.; Wollscheid, U.; Momburg, F.; Blankenstein, T.; Huber, C.
CORPORATE SOURCE: Johannes Gutenberg Universitat, III. Medizinische Klinik, Mainz, 55131, Germany
SOURCE: Tissue Antigens (2000), 56(4), 327-336
CODEN: TSANA2; ISSN: 0001-2815
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In murine **tumor** cell lines, downregulation of MHC class I surface expression has been frequently detected, but the underlying mol. mechanisms of such deficiencies have not been defined. In this study, murine **tumor** cell lines of different histol. derived from spontaneous or from chem.-induced **tumors** were analyzed for the expression of multiple components of the major histocompatibility complex (MHC) class I antigen-processing machinery (APM), including the peptide transporter TAP, the interferon (IFN)-.gamma. inducible proteasome subunits and several chaperones. The **tumor** cell lines analyzed demonstrated a heterogeneous expression pattern of various APM components. In comparison to control cells an impaired coordinated expression of at least three APM components was detected. In particular, extensive APM deficiencies were found in cell lines derived from chem.-induced **tumors**. A strong coordinated downregulation of expression and/or function of TAP, the low mol. wt. proteins (LMP) subunits, the proteasome activator PA28 and/or tapasin was found in 5 of 10 **tumor** cells, which was assocd. with impaired MHC class I surface expression. In contrast, the expression of .beta.2-microglobulin (.beta.2-m), PA28.beta., the constitutive proteasome subunits X, Y, Z and of the chaperones calnexin, **calreticulin**, ER60 and phospho disulfide isomerase (PDI) was unaltered or only weakly decreased. The deficient expression of APM components could be cor. by IFN-.gamma. **treatment**, which also reconstituted MHC class I surface expression. However, impaired expression of APM mols. appears not to be the only cause of abnormal MHC class 1 expression, since it could neither be cor. by the addn. of exogenous MHC class I binding peptides nor by incubation at low temp. These results suggest that one major mechanism of murine **tumor** cells, in particular chem.-induced **tumors**, to evade the immune system is the combined dysregulation of various APM components and other factors, which still have to be identified.

REFERENCE COUNT: 49
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:706994 HCAPLUS
DOCUMENT NUMBER: 133:286473
TITLE: Compositions and methods for producing platelets and/or proplatelets from megakaryocytes
INVENTOR(S): Loscalzo, Joseph; Battinelli, Elisabeth M.
PATENT ASSIGNEE(S): Trustees of Boston University, USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000057891	A1	20001005	WO 2000-US6436	20000330	

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-126854 P 19990330
OTHER SOURCE(S): MARPAT 133:286473

AB The present invention describes novel compns. and methods to enhance the in vitro and in vivo prodn. of platelets and/or proplatelets from megakaryocytes. The present invention describes compns. comprising megakaryocytes, nitric oxide donors (i.e. compds. that donate, transfer or release nitric oxide, elevate endogenous levels of **endothelium** -derived relaxing factor, stimulate endogenous synthesis of nitric oxide or are substrates for nitric oxide synthase), and, optionally, at least one thrombopoiesis stimulating factor. The thrombopoiesis stimulating factor is preferably thrombopoietin. The nitric oxide donor is preferable S-nitrosoglutathione. The present invention also describes compns. comprising at least one nitric oxide donor and at least one thrombopoiesis stimulating factor. The present invention also provides methods for **treating** and/or **preventing** blood platelet disorders, and for producing platelets and/or proplatelets in vitro and in vivo. The compds. and/or compns. of the present invention can be provided in the form of a pharmaceutical kit.

REFERENCE COUNT: 3
REFERENCE(S):
(1) Barrett; US 5932546 A 1999 HCAPLUS
(2) Bolton; US 5834030 A 1998 HCAPLUS
(3) The Wellcome Foundation Limited; WO 9616645 A1 1996 HCAPLUS

L4 ANSWER 15 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:608612 HCAPLUS
DOCUMENT NUMBER: 133:206756
TITLE: Compositions and methods using complexes of **calreticulin** and antigenic molecules
INVENTOR(S): Gilboa, Eli; Nair, Smita K.; Nicchitta, Christopher V.
PATENT ASSIGNEE(S): Duke University, USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050080	A1	20000831	WO 2000-US4565	20000223

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,

IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 1999-261473 A 19990226
AB A method of eliciting an immune response in a vertebrate subject. The method includes the administration to a vertebrate subject of a compn. including an amt. of a purified complex including **calreticulin** bound to an antigenic mol. to elicit an immune response to the antigenic mol. in the vertebrate subject. Therapeutic methods, compns. and kits are also disclosed wherein the elicited immune response is utilized as a **treatment** for **cancer** and for infectious diseases.

L4 ANSWER 16 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:521385 HCAPLUS
DOCUMENT NUMBER: 133:217893
TITLE: Unliganded and liganded estrogen receptors protect against cancer invasion via different mechanisms
AUTHOR(S): Platet, Nadine; Cunat, Severine; Chalbos, Dany; Rochefort, Henri; Garcia, Marcel
CORPORATE SOURCE: Institut National de la Sante et de la Recherche Medicale Unite Hormones et Cancer (U148) and Universite de Montpellier I, Montpellier, 34090, Fr.
SOURCE: Mol. Endocrinol. (2000), 14(7), 999-1009
CODEN: MOENEN; ISSN: 0888-8809
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB While estrogens are mitogenic in breast **cancer** cells, the presence of estrogen receptor .alpha. (ER.alpha.) clin. indicates a favorable prognosis in breast **carcinoma**. To improve our understanding of ER.alpha. action in breast **cancer**, we used an original in vitro method, which combines transient transfection and Matrigel invasion assays to examine its effects on cell invasiveness. ER.alpha. expression in MDA-MB-231 breast **cancer** cells reduced their invasiveness by 3-fold in the absence of hormone and by 7-fold in its presence. Integrity of hormone and DNA-binding domains and activating function 2 were required for estradiol-induced **inhibition**, suggesting that transcriptional activation of estrogen target genes was involved. In contrast, these domains were dispensable for hormone-independent **inhibition**. Anal. of deletion mutants of ER.alpha. indicated that amino acids 179-215, contg. the N-terminal zinc finger of the DNA-binding domain, were required for ligand-independent receptor action. Among different members of the nuclear receptor family, only unliganded ER.alpha. and ER.beta. reduced invasion. **Calreticulin**, a Ca2+-binding protein that could interact with amino acids 206-211 of ER.alpha., reversed hormone-independent ER.alpha. **inhibition** of invasion. However, since **calreticulin** alone also **inhibited** invasion, we propose that this protein probably **prevents** ER.alpha. interaction with another unidentified invasion-regulating factor. The **inhibitor** role of

the unliganded ER was also suggested in three ER.alpha.-pos. cell lines, where ER.alpha. content was inversely correlated with cell migration. We conclude that ER.alpha. protects against **cancer** invasion in its unliganded form, probably by protein-protein interactions with the N-terminal zinc finger region, and after hormone binding by activation of specific gene transcription.

REFERENCE COUNT: 50
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:351546 HCAPLUS
DOCUMENT NUMBER: 133:13447
TITLE: A regulatory element in genes for chaperonins of the endoplasmic reticulum involved in stress induction of gene expression
INVENTOR(S): Haze, Kyosuke; Yoshida, Hiderou; Mori, Kazutoshi; Yanagi, Hideki; Yura, Takashi
PATENT ASSIGNEE(S): HSP Research Institute, Inc., Japan
SOURCE: PCT Int. Appl., 157 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000029429	A2	20000525	WO 1999-JP6305	19991112
WO 2000029429	A3	20001109		
W: CA, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 2001054391	A2	20010227	JP 1999-321743	19991111
EP 1131435	A2	20010912	EP 1999-972220	19991112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: JP 1998-324227 A 19981113
JP 1999-163112 A 19990609
WO 1999-JP6305 W 19991112

AB A regulatory element that plays a role in the induction and repression of expression of genes for chaperonins of the endoplasmic reticulum is described. The element can be used to regulate the expression of foreign genes in animal cells. The element, ERSE (endoplasmic reticulum stress element) is regulated by the transcription factors ATF-6 and CREB-BP. It is expected to be applied to **treatment** or prophylaxis of **cancers**, arteriosclerosis, cystic fibrosis, ischemic diseases, wounds or ulcers. The element was identified in the human GRP78 promoter by deletion and point mutation anal. Similar sequences were found in the

genes for GRP94 and **calreticulin**. Genes encoding transcription factors interacting with ERSE were identified using single hybrid anal. ATF6 was found to be synthesized as an inactive precursor that was activated by proteolytic cleavage during stress. CREB-BP was also found to be synthesized as an inactive precursor that was activated by proteolytic cleavage during stress. N-terminal deletion derivs. of ATF6 and CREB-RP suppress ERSE-dependent gene expression.

L4 ANSWER 18 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:242976 HCAPLUS
DOCUMENT NUMBER: 133:236554
TITLE: Immunoprotective activities of multiple chaperone proteins isolated from murine B-cell leukemia/lymphoma
AUTHOR(S): Graner, Michael; Raymond, Amy; Romney, Davis; He, Lin; Whitesell, Luke; Katsanis, Emmanuel
CORPORATE SOURCE: Department of Pediatrics, Steele Memorial Children's Research Center, University of Arizona, Tucson, AZ, 85724-5073, USA
SOURCE: Clin. Cancer Res. (2000), 6(3), 909-915
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Although the use of **tumor**-derived heat shock/chaperone proteins (HSPs) as **anticancer** vaccines is gaining wider study and acceptance, there have thus far been no reports concerning chaperone **antitumor** activities against disseminated hematol. malignancies. We have devised an efficient and effective method for purifn. of the chaperone proteins grp94/gp96, HSP90, HSP70, and **calreticulin** from harvested A20 murine **leukemia/lymphoma** **tumor** material. We have demonstrated that these purified proteins, when used as vaccines, can induce potent and specific immunity against a lethal **tumor** challenge. Individual chaperone proteins were differentially effective in their abilities to provide immune protection. The increase in survival generated by the most effective chaperone vaccine, HSP70, resulted from at least a 2-log redn. in **tumor** burden. Syngeneic granulocyte macrophage colony-stimulating factor producing fibroblasts were injected at the site of vaccination in an attempt to augment the immune response. Surprisingly, localized granulocyte macrophage colony-stimulating factor prodn. **inhibited** the protective effects of chaperone vaccination. These studies provide evidence that chaperone proteins can be isolated from B-cell **tumors** and used effectively to immunize against disseminated lymphoid malignancies.
REFERENCE COUNT: 40
REFERENCE(S): (1) Arnold, D; J Exp Med 1995, V182, P885 HCAPLUS
(2) Arnold-Schild, D; J Immunol 1999, V162, P3757 HCAPLUS
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(5) Bronte, V; J Immunol 1999, V162, P5728 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 51 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:241470 HCAPLUS
DOCUMENT NUMBER: 132:288763
TITLE: Use of **calreticulin** and **calreticulin** fragments to **inhibit endothelial** cell **growth** and **angiogenesis**, and suppress **tumor growth**
INVENTOR(S): Tosato, Giovanna; Pike, Sandra; Yao, Lei
PATENT ASSIGNEE(S): The Government of the United States of America, Represented by the Secretary, USA
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000020577	A1	20000413	WO 1999-US23240	19991005
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, ZA, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9962917	A1	20000426	AU 1999-62917	19991005

PRIORITY APPLN. INFO.: US 1998-103438 P 19981006
WO 1999-US23240 W 19991005

AB Methods for **inhibiting endothelial** cell **growth** and **angiogenesis** and for suppressing **tumor growth** using **calreticulin**, fragments of **calreticulin**, and variants of **calreticulin** are provided. Such methods are useful for the **treatment** of **cancer** and diseases assocd. with unwanted **angiogenesis**, e.g., chronic retinal detachment. Thus, **calreticulin** was shown to exhibit three previously uncharacterized biol. activities. First, **calreticulin inhibited endothelial** cell **growth** while having little or no effect on the **growth** of non-**endothelial** cells. Second, **calreticulin inhibited angiogenesis**. Third, **calreticulin inhibited tumor growth**, including **growth** of Burkitt's **lymphoma**, breast **adenocarcinoma**, colon **carcinoma**, lung **carcinoma**, **melanoma**, **rhabdomyosarcoma**, promyelomonocytic **lymphoma**, Wilm's **tumor**, and neuroblastoma. Certain fragments of **calreticulin**, e.g., **calreticulin** lacking the N-terminal 120 amino acids, the N-terminal domain (amino acids 1-180), and fragments of this N-terminal domain, were found to share these activities.

IT **144713-91-7, Calreticulin** (human clone Ro38-1 protein moiety reduced)

RL: BAC (Biological activity or effector, except adverse); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; use of **calreticulin** and **calreticulin** fragments to **inhibit endothelial** cell **growth** and **angiogenesis**, and suppress **tumor growth**)

IT **144713-90-6, Calreticulin** (human clone Ro38-1 precursor protein moiety reduced)
RL: PRP (Properties)
(unclaimed protein sequence; use of **calreticulin** and **calreticulin** fragments to **inhibit endothelial** cell **growth** and **angiogenesis**, and suppress **tumor growth**)

REFERENCE COUNT: 11
REFERENCE(S):
(1) Dai, E; ARTERIOSCLEROSIS, THROMBOSIS AND VASCULAR BIOLOGY 1997, V17(11), P2359 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:134362 HCAPLUS
DOCUMENT NUMBER: 132:291275
TITLE: Genes dependent on zebrafish cyclops function identified by AFLP differential gene expression screen
AUTHOR(S): Rubinstein, Amy L.; Lee, Danny; Luo, Rushu; Henion, Paul D.; Halpern, Marnie E.
CORPORATE SOURCE: Department of Embryology, Carnegie Institution of Washington, Baltimore, MD, 21210, USA
SOURCE: Genesis (N. Y.) (2000), 26(1), 86-97
CODEN: GNESFY; ISSN: 1526-954X
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Zebrafish cyclops (cyc) encodes a transforming **growth** factor .beta. (TGF.beta.) signaling factor closely related to mouse Nodal. By comparing amplified fragment length polymorphisms (AFLP) from cyc mutant and wildtype cDNA pools, we devised a differential gene expression screen to isolate genes whose expression is dependent on Cyc signaling. We report 2 genes not previously described in the zebrafish that were identified using this approach. The 1st gene, crestin, is expressed predominantly in premigratory and migrating neural crest cells during somitogenesis stages. Crestin expression is reduced in cyc mutants initially but recovers by late somitogenesis. The 2nd gene encodes the zebrafish homolog of the calcium-binding protein, **calreticulin**. Zebrafish **calreticulin** is highly expressed in the hatching gland and in the floor plate, tissues that are affected in cyc mutants. During gastrulation, **calreticulin** transcripts are found in the dorsal mesendoderm, in the same cells that express the cyc gene. Expression is reduced in cyc mutants and is abolished by the one-eyed pinhead (oep) mutation that is presumed to **prevent** Nodal signaling. The

identification of **calreticulin** suggests that a differential screen between wild-type and mutant cDNA is a useful approach to reveal regulation of unexpected gene expression in response to cellular signals.

IT **264868-11-3, Calreticulin** (Danio rerio)
RL: BOC (Biological occurrence); BPR (Biological process); MFM (Metabolic formation); PRP (Properties); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PROC (Process)
(amino acid sequence; **calreticulin** and crestin protein sequence and cyclops-regulated expression in zebrafish embryos)

REFERENCE COUNT: 75
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:644147 HCAPLUS
DOCUMENT NUMBER: 131:331844
TITLE: **Calreticulin** and **calreticulin** fragments are **endothelial** cell **inhibitors** that suppress **tumor growth**
AUTHOR(S): Pike, Sandra E.; Yao, Lei; Setsuda, Joyce; Jones, Karen D.; Cherney, Barry; Appella, Ettore; Sakaguchi, Kazuyasu; Nakhasi, Hira; Atreya, Chintamani D.; Teruya-Feldstein, Julie; Wirth, Peter; Gupta, Ghanshyam; Tosato, Giovanna
CORPORATE SOURCE: Center for Biologics Evaluation and Research, Rockville, MD, 20852, USA
SOURCE: Blood (1999), 94(7), 2461-2468
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several **angiogenesis inhibitors** are fragments of larger proteins that are themselves not active as **angiogenesis inhibitors**. Vasostatin, the N-terminal domain of **calreticulin** inclusive of amino acids 1-180, is an **angiogenesis inhibitor** that exerts **antitumor** effects in vivo. In the present study, we examd. whether the full-length **calreticulin** mol. shares the antiangiogenic and **antitumor** activities of vasostatin. Similar to vasostatin, **calreticulin** selectively **inhibited endothelial** cell proliferation in vitro, but not cells of other lineages, and suppressed **angiogenesis** in vivo. When inoculated into athymic mice, **calreticulin inhibited** Burkitt **tumor growth** comparably with vasostatin. **Calreticulin** lacking the N-terminal 1-120 amino acids **inhibited endothelial** cell proliferation in vitro and Burkitt **tumor growth** in vivo comparably with vasostatin. An internal **calreticulin** fragment encompassing amino acids 120-180 also **inhibited**

endothelial cell proliferation in vitro and **angiogenesis** in vivo comparably with **calreticulin** and vasostatin. These results suggest that the antiangiogenic activities of vasostatin reside in a domain that is accessible from the full-length **calreticulin** mol. and localize to **calreticulin** N-terminal amino acids 120-180. Thus, **calreticulin** and **calreticulin** fragments are **inhibitors** of **angiogenesis** that directly target **endothelial** cells, **inhibit angiogenesis**, and suppress **tumor growth**. This information may be crit. in designing targeted **inhibitors** of pathol. **angiogenesis** that underlies **cancer** and other diseases.

REFERENCE COUNT: 41
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:561437 HCAPLUS
DOCUMENT NUMBER: 132:77347
TITLE: Generation of a monoclonal antibody against human **calreticulin** by immunization with a recombinant **calreticulin** fusion protein: application in paraffin-embedded sections
AUTHOR(S): Cavill, Dana; Macardle, Peter J.; Beroukas, Dimitra; Kinoshita, Gentaro; Stahl, Jurgen; McCluskey, James; Gordon, Tom P.
CORPORATE SOURCE: Departments of Immunology, Allergy & Arthritis, University of Melbourne, Victoria, Australia
SOURCE: Appl. Immunohistochem. Mol. Morphol. (1999), 7(2), 150-155
CODEN: AIMMFN
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Calreticulin** (CR) is a highly conserved, calcium-binding protein with a diverse functional repertoire located primarily in the endoplasmic reticulum (ER). A murine monoclonal antibody (mAb) reactive with human CR was produced by immunizing with a maltose-binding protein-CR fusion protein expressed in Escherichia coli. This mAb (FMC75) bound recombinant and native human 60-kDa CR on Western blots but, unlike a polyclonal anti-CR antibody, did not cross-react with mouse CR. FMC75 gave a staining pattern identical to that of the polyclonal antibody on confocal microscopy of cultured cells and was pos. on microwave-**treated** tissue sections embedded in paraffin. Immunohistochem. anal. of a range of normal tissues confirmed the widespread expression of CR, notably in parenchymal epithelial cells, neurons, **endothelial** cells, and lymphocytes, predominantly of B-cell origin. The pattern of staining was cytoplasmic, not nuclear. Only weak staining was found in stromal cells. This first mAb to be produced against human CR will be a valuable reagent for studying the expression of CR and its putative role in autoimmune disease and malignancy. Recombinant fusion proteins in which the target

protein is fused with a foreign moiety may be useful immunogens for breaking tolerance and generating mAbs against extremely conserved proteins such as CR.

REFERENCE COUNT: 9

REFERENCE(S):
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(9) Zhu, N; Endocrinology 1998, V139, P4337 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:532898 HCAPLUS
DOCUMENT NUMBER: 131:269858
TITLE: Roles of **calreticulin** and calnexin during mucin synthesis in LS180 and HT29/A1 human colonic adenocarcinoma cells
AUTHOR(S): McCool, Dorothy J.; Okada, Yoshio; Forstner, Janet F.; Forstner, Gordon G.
CORPORATE SOURCE: Research Institute. The Hospital for Sick Children and the Department of Biochemistry, University of Toronto, Toronto, ON, M5G 1X8, Can.
SOURCE: Biochem. J. (1999), 341(3), 593-600
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mol. chaperones are presumed to assoc. with large secretory mucin glycoproteins during their synthesis in the endoplasmic reticulum (ER), but have not been identified to date. We decided to look for possible involvement of the chaperones **calreticulin** (CRT) and calnexin (CLN) during synthesis of two similar gastrointestinal mucins, MUC2 and MUC5AC. Pulse-chase labeling of MUC2 and MUC5AC with [35S]methionine/cysteine ([35S]Promix) was performed using LS180 and HT29/A1 colonic **carcinoma** cell lines and was followed by immunopptn. with anti-mucin and anti-chaperone antibodies. The pptd. labeled mucin precursors were analyzed by SDS-PAGE and autoradiog. Using antibodies specific for each mucin, newly synthesized monomeric precursors of both MUC2 and MUC5AC were detected after a 15 min pulse and then disappeared as oligomers were formed during a 2 h chase period. Only homo-oligomers of MUC2 and MUC5AC were present in the cells. Using anti-CRT, the MUC2 monomeric precursor and oligomer were co-pptd. from both cell lines after a 15 min pulse and the oligomer less strongly after a 0.5 h chase, but there was little co-pptn. after a 2 h chase. At this time, MUC2 immunopptd. by anti-MUC2 was completely oligomerized and was endo-.beta.-N-acetylglucosaminidase-resistant, indicating that the mucin had reached the Golgi region. MUC2 co-pptd. with CRT at zero time and 0.5 h was endo-.beta.-N-acetylglucosaminidase-sensitive; therefore CRT must have assocd. with MUC2 in the ER. **Treatment** with tunicamycin (TUN) diminished the binding of MUC2 to CRT, suggesting a requirement for initial N-glycan addn. during this process. Using anti-CLN, only a weak co-pptn. of MUC2, compared with that seen with anti-CRT, was detected in

LS180 cells. In contrast with the findings for MUC2, there was no co-pptn. of MUC5AC with CRT or CLN from either cell line at the various time points. In conclusion, CRT and CLN appear to be involved in MUC2 synthesis at the stage of folding and oligomerization in the ER. Since no interaction of the chaperones with MUC5AC was detected at a similar stage of synthesis, these two structurally similar secretory mucins seem to have different chaperone requirements in the ER.

REFERENCE COUNT: 47

REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:369691 HCAPLUS
DOCUMENT NUMBER: 131:142586
TITLE: Ligand-specific, transient interaction between integrins and **calreticulin** during cell adhesion to extracellular matrix proteins is dependent upon phosphorylation/dephosphorylation events
AUTHOR(S): Coppolino, Marc G.; Dedhar, Shoukat
CORPORATE SOURCE: Department of Cell Biology, Hospital for Sick Children, Toronto, ON, M5G 1X8, Can.
SOURCE: Biochem. J. (1999), 340(1), 41-50
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB As transmembrane heterodimers, integrins bind to both extracellular ligands and intracellular proteins. We are currently investigating the interaction between integrins and the intracellular protein **calreticulin**. A prostatic **carcinoma** cell line (PC-3) was used to demonstrate that **calreticulin** can be found in the .alpha.3 immunoppts. of cells plated on collagen type IV, but not when plated on vitronectin. Conversely, .alpha.v immunoppts. contained **calreticulin** only when cells were plated on vitronectin, i.e. not when plated on collagen IV. The interactions between these integrins and **calreticulin** were independent of actin cytoskeleton assembly and were transient, being maximal approx. 10-30 min after the cells came into contact with the substrates prior to complete cell spreading and formation of firm adhesive contacts. We demonstrate that okadaic acid, an **inhibitor** of intracellular serine/threonine protein phosphatases, **inhibited** the .alpha.3.beta.1-mediated adhesion of PC-3 cells to collagen IV and the .alpha.2.beta.1-mediated attachment of Jurkat cells to collagen I. This **inhibition** by okadaic acid was accompanied by **inhibition** of the ligand-specific interaction of **calreticulin** with the resp. integrins in the two cell types. Addnl., we found that pharmacol. **inhibition** of mitogen-activated protein kinase kinase (MEK) resulted in prolongation of the **calreticulin**-integrin interaction, and enhancement of PC-3 cell attachment to collagen IV. We conclude that **calreticulin** interacts transiently with integrins during cell attachment and spreading.

This interaction depends on receptor occupation, is ligand-specific, and can be modulated by protein phosphatase and MEK activity.

REFERENCE COUNT: 52

REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 51 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:273044 HCAPLUS

DOCUMENT NUMBER: 131:57183

TITLE: **Calreticulin** expression is associated with androgen regulation of the sensitivity to calcium ionophore-induced apoptosis in LNCaP prostate cancer cells

AUTHOR(S): Zhu, Ning; Wang, Zhou

CORPORATE SOURCE: Department of Urology, Northwestern University Medical School, Chicago, IL, 60611, USA

SOURCE: Cancer Res. (1999), 59(8), 1896-1902
CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: AACR Subscription Office

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Calreticulin** has been identified previously as one of the androgen-response genes in the prostate. The role of **calreticulin** in androgen action was studied using androgen-sensitive LNCaP and androgen-insensitive PC-3 human prostate **cancer** cell lines. **Calreticulin** appears to be a primary androgen-response gene in cultured LNCaP cells because androgen induction of **calreticulin** mRNA resists protein synthesis **inhibition**. **Calreticulin** is a high capacity intracellular Ca2+ binding protein, suggesting that **calreticulin** expression is likely to be assocd. with the intracellular Ca2+ buffering capacity that could regulate the sensitivity to cytotoxic intracellular Ca2+ overload. As expected, androgen protects androgen-sensitive LNCaP but not androgen-insensitive PC-3 cells from cytotoxic intracellular Ca2+ overload induced by Ca2+ ionophore A23187. To provide evidence for the role of **calreticulin** in reducing cytotoxic effect of Ca2+ influx in prostatic cells, we have shown that **calreticulin** antisense oligonucleotide down-regulates **calreticulin** protein level and significantly increases the sensitivity to A23187-induced apoptosis in both LNCaP and PC-3 cells. Furthermore, **calreticulin** antisense oligonucleotide reverses the androgen-induced resistance to A23187 in LNCaP cells. The above observations collectively suggest that **calreticulin** mediates androgen regulation of the sensitivity to Ca2+ ionophore-induced apoptosis in LNCaP cells.

REFERENCE COUNT: 29

REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 26 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:244758 HCAPLUS
DOCUMENT NUMBER: 130:280309
TITLE: Proteins and nucleic acids associated with human prostate cancer and methods for immunotherapy and immunodiagnosis of prostate cancer
INVENTOR(S): Reed, Steven G.; Dillon, Davin C.; Twardzik, Daniel R.; Mitcham, Jennifer L.
PATENT ASSIGNEE(S): Corixa Corporation, USA
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9918210	A2	19990415	WO 1998-US21166	19981007
WO 9918210	A3	19990805		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6034218	A	20000307	US 1997-946026	19971007
AU 9896893	A1	19990427	AU 1998-96893	19981007

PRIORITY APPLN. INFO.:

US 1997-946026	A	19971007
US 1996-616745	B2	19960315
US 1996-633840	B2	19960411
US 1998-102679	A	19980623
WO 1998-US21166	W	19981007

AB Compds. and methods for **treating** and diagnosing prostate **cancer** are provided. The inventive compds. include polypeptides contg. at least a portion of a prostate protein. Polypeptide fragments and their encoding cDNAs were isolated and characterized from a suitable human prostate **adenocarcinoma** cell line, such as LnCap.fgc (ATCC 1740-CRL), by screening with human, rat, and monkey prostatitis sera or with prostate **tumor**-specific monoclonal antibodies. Vaccines and pharmaceutical compns. for immunotherapy of prostate **cancer** comprising such polypeptides or DNA mols. encoding such polypeptides are also provided. The inventive polypeptides may also be used to generate antibodies useful for the diagnosis and monitoring of prostate **cancer**. Nucleic acid sequences for prepg. probes, primers, and

polypeptides are also provided.

L4 ANSWER 27 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:96269 HCAPLUS
DOCUMENT NUMBER: 130:148717
TITLE: Pharmaceutical compositions containing proteins or peptides for modulating hormone responsiveness
INVENTOR(S): Dedhar, Shoukat; Doersen, Claus-Jens Walter; Mazur, Adam Weislaw
PATENT ASSIGNEE(S): Can.
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9905172	A2	19990204	WO 1998-CA715	19980724
WO 9905172	A3	19990415		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 5854202	A	19981229	US 1995-377432	19950124
AU 9885251	A1	19990216	AU 1998-85251	19980724
EP 1001986	A2	20000524	EP 1998-936040	19980724
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 9945861	A1	19991028	AU 1999-45861	19990901

PRIORITY APPLN. INFO.:
US 1995-377432 A2 19950124
US 1997-900241 A2 19970724
AU 1995-39203 A3 19951123
WO 1998-CA715 W 19980724

OTHER SOURCE(S): MARPAT 130:148717

AB This invention relates to isolated and purified proteins, such as **calreticulin** and mimetics and **inhibitors** of **calreticulin**, for a novel use of modulating hormone responsiveness. These proteins are useful in gene therapy and in manufg. pharmaceuticals for **treating** a variety of diseases, including **cancer**, osteoporosis and chronic inflammatory disease. The proteins include or bind to an amino acid sequence [SEQ ID NO: 1] KXFFX1R (X = G, A, V; X1 = K, R). This sequence is present in the DNA-binding domain, and is crit. for the DNA binding activity, of a variety of hormone receptors, including glucocorticoid receptor, mineralocorticoid receptor, androgen receptor, progesterone receptor, estrogen receptor, retinoic acid receptor, thyroid hormone receptor and vitamin D receptor. Proteins which bind to this sequence may **inhibit** hormone receptor induced gene transcription. Proteins which include this sequence may promote hormone

receptor induced gene transcription. The invention includes isolated DNA mols. for these proteins, methods of **treating** diseases using these proteins, synthetic peptides or their mimetics.

L4 ANSWER 28 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:11304 HCAPLUS
DOCUMENT NUMBER: 130:177891
TITLE: Vasostatin, a **calreticulin** fragment, **inhibits angiogenesis** and suppresses **tumor growth**
AUTHOR(S): Pike, Sandra E.; Yao, Lei; Jones, Karen D.; Cherney, Barry; Appella, Ettore; Sakaguchi, Kazuyasu; Nakhasi, Hira; Teruya-Feldstein, Julie; Wirth, Peter; Gupta, Ghanshyam; Tosato, Giovanna
CORPORATE SOURCE: Center for Biologics Evaluation and Research, Rockville, MD, 20852, USA
SOURCE: J. Exp. Med. (1998), 188(12), 2349-2356
CODEN: JEMEAV; ISSN: 0022-1007
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An **endothelial** cell **inhibitor** was purified from supernatant of an Epstein-Barr virus-immortalized cell line and identified as fragments of **calreticulin**. The purified recombinant NH2-terminal domain of **calreticulin** (amino acids 1-180) **inhibited** the proliferation of **endothelial** cells, but not cells of other lineages, and suppressed **angiogenesis** in vivo. We have named this NH2-terminal domain of **calreticulin** vasostatin. When inoculated into athymic mice, vasostatin significantly reduced **growth** of human Burkitt **lymphoma** and human colon **carcinoma**. Compared with other **inhibitors** of **angiogenesis**, vasostatin is a small, sol., and stable mol. that is easy to produce and deliver. As an **angiogenesis inhibitor** that specifically targets proliferating **endothelial** cells, vasostatin has a unique potential for **cancer treatment**.
REFERENCE COUNT: 46
REFERENCE(S): (1) Angiolillo, A; J Exp Med 1995, V182, P155 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 29 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:812027 HCAPLUS
DOCUMENT NUMBER: 130:166966
TITLE: The first subcomponent of complement, C1q, triggers the production of IL-8, IL-6, and monocyte chemoattractant peptide-1 by human umbilical vein endothelial cells
AUTHOR(S): Van den Berg, Rocco H.; Faber-Krol, Maria C.; Sim, Robert B.; Daha, Mohamed R.
CORPORATE SOURCE: Dep. Nephrol., Leiden Univ. Hosp., Leiden, Neth.

SOURCE: J. Immunol. (1998), 161(12), 6924-6930
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We and others have demonstrated previously the occurrence of cC1qR/CaR, a receptor for the collagen-like stalks of complement component C1q, on **endothelial** cells. In the present study we investigated whether binding of C1q to **endothelial** cells resulted in enhancement of cytokine or chemokine prodn. HUVEC produced 82.+-.91 pg/mL of IL-8, 79.+-.113 pg/mL of IL-6, and 503.+-.221 pg/mL of monocyte chemoattractant peptide-1 (MCP-1) under basal conditions. Incubation with C1q resulted in a time- and dose-dependent on de novo protein synthesis, as demonstrated by the detection of specific mRNA after C1q stimulation, and **inhibition** of peptide prodn. in the presence of cycloheximide. The prodn. of all factors was **inhibited** (69.+-.7%) by the collagenous fragments of C1q, while the C1q globular heads only induced 13.+-.11% **inhibition**. When HUVEC were incubated with C1q in the presence of aggregated IgM, enhanced prodn. of IL-8 (2500.+-.422 pg/mL), IL-6 (997.+-. 21 pg/mL), and MCP-1 (5343.+-.302 pg/mL) was found. Furthermore, F(ab')2 anti-**calreticulin** partially **inhibited** the prodn. of IL-8, confirming at least the involvement of cC1qR/CaR. These expts. suggest that in an inflammatory response C1q not only is able to activate the complement pathway, but when presented in a proper fashion also might induce the prodn. of factors that contribute to acute phase responses and recruitment of inflammatory cells.

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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 30 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:640363 HCAPLUS
DOCUMENT NUMBER: 129:258972
TITLE: Identification of **tumor**-associated alleles of genes essential for cell viability and **growth** and the development of **neoplasm inhibitors** targetted against them
INVENTOR(S): Housman, David; Ledley, Fred D.; Stanton, Vincent P., Jr.
PATENT ASSIGNEE(S): Variagenics, Inc., USA
SOURCE: PCT Int. Appl., 605 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9841648 A2 19980924 WO 1998-US5419 19980319
WO 9841648 A3 19990429
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
AU 9867643 A1 19981012 AU 1998-67643 19980319
EP 973935 A2 20000126 EP 1998-912974 19980319
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRIORITY APPLN. INFO.: US 1997-41057 19970320
WO 1998-US5419 19980319

AB Strategies for the identification and targeting of specific alleles of genes in the **treatment** of **tumors** are described. **Tumor**-assocd. alleles of genes coding for proteins essential for cell viability or cell **growth** and that show loss of an alleles in **cancer** cells due to loss of heterozygosity (LOH) are identified. **Inhibitors** of the remaining allele, such as antisense nucleic acids or ribozymes, can then be developed. The method can also be used to **inhibit** the expression of particular alleles of genes for antigens in the control of transplant rejection. Particular categories of appropriate target genes are described, along with specific exemplary genes within those categories and methods of using such target genes. Antisense phosphorothioate oligonucleotides targeting RNA polymerase II and glutamyl/prolyl tRNA synthetase genes were tested for cytotoxicity in vitro. Oligonucleotides with a single base mismatch were significantly less toxic than those without mismatches. A no. of genes essential for proliferation were mapped and shown to be affected by loss-of-heterozygosity in oncogenesis.

L4 ANSWER 31 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:568937 HCAPLUS
DOCUMENT NUMBER: 129:200685
TITLE: Increasing plant growth rates by increasing the rate of the dark reaction of photosynthesis
INVENTOR(S): Basel, Richard M.; Elion, Glenn R.
PATENT ASSIGNEE(S): Agricola Technologies, Inc., USA
SOURCE: PCT Int. Appl., 143 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9836084	A2	19980820	WO 1998-US2501	19980206
WO 9836084	A3	19981217		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,

UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9861529 A1 19980908 AU 1998-61529 19980206
PRIORITY APPLN. INFO.: US 1997-801120 19970214
WO 1998-US2501 19980206

AB Methods of increasing rates of plant **growth** by **preventing** the dark reaction of photosynthesis from being rate limiting are described. This is achieved by increasing the efficiency of uptake and transport of carbon dioxide as carbonate using an animal carbonic anhydrase or by ensuring adequate pools of cofactors or other metabolites. Metal ion cofactors, such as Ca2+ and Zn2+, can be stored as complexes with metal binding proteins and phosphate can be stored in biomineralization proteins. The genes may be of microbial, plant or animal (specifically mammalian) origin. Tobacco plants transformed with a human carbonic anhydrase II gene under control of a 35S promoter showed faster **growth** than control plants. Similar, although less marked, effects were seen with genes for calcium-binding or hydroxyapatite-nucleating proteins. The effects of the genes were synergistic with the calcium-binding proteins also increasing plant calcium content approx. 10-fold without calcium supplementation of **growth** media. Expression of a metallothionein expression construct into potato increased **growth** rates and also plant resistance to cadmium.

L4 ANSWER 32 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:471187 HCAPLUS
DOCUMENT NUMBER: 129:228672
TITLE: Placental 57-kDa Ca2+-binding protein: regulation of expression and function in trophoblast calcium transport
AUTHOR(S): Hershberger, Marcia E.; Tuan, Rocky S.
CORPORATE SOURCE: Department of Orthopaedic Surgery, Thomas Jefferson University, Philadelphia, PA, 19107, USA
SOURCE: Dev. Biol. (1998), 199(1), 80-92
CODEN: DEBIAO; ISSN: 0012-1606
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB During gestation, transport by placental trophoblasts is solely responsible for nutrient supply to the developing fetus. The calcium (Ca) transport machinery of the placenta thus represents the primary tissue site for regulating fetal Ca homeostasis. The exact mechanism of trophoblast Ca transport is not known. However, there is evidence suggesting that a developmentally expressed cytosolic, trophoblast-specific, high Mr 57-kDa Ca-binding protein (CaBP) plays an important role in regulating and/or shuttling cytosolic Ca. The authors report the cloning of a full-length cDNA of the mouse CaBP which shows significant homol. with **calreticulin**, an endoplasmic reticulum-assocd. Ca binding protein. The functional role of CaBP in cellular Ca handling was investigated using a trophoblastic cell line, Rcho-1, derived from a rat **choriocarcinoma**. Upon differentiation, Rcho-1 cells exhibit enhanced Ca uptake compared to

undifferentiated Rcho-1 stem cells, and CaBP expression is upregulated. To analyze the regulation of CaBP expression, placenta organ cultures and Rcho-1 cells were **treated** for 48 h in vitro with a series of agents implicated in Ca homeostasis. In both placenta organ cultures and undifferentiated as well as differentiated Rcho-1 cells, **treatment** with 1,25-dihydroxy vitamin D3, estrogen, parathyroid hormone (PTH), parathyroid hormone-related protein (PTHrP 1-34), and Ca had no effect on CaBP mRNA and protein levels, which were significantly stimulated by PTHrP 67-84. PTHrP 67-84-**treated** Rcho-1 cells also exhibited higher Ca uptake activity than untreated control cells. The upregulation of CaBP expression during and/or following the differentiation of Rcho-1 cells into trophoblastic giant cells supports the importance of CaBP in trophoblast maturation and the validity of the Rcho-1 rat model cell system. In addn., the action of PTHrP on placental trophoblast Ca transport is likely to involve the regulation of CaBP expression to handle the increasing Ca requirements of the developing fetus. (c) 1998 Academic Press.

L4 ANSWER 33 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:285023 HCAPLUS
DOCUMENT NUMBER: 129:49886
TITLE: Folding of insulin receptor monomers is facilitated by the molecular chaperones calnexin and **calreticulin** and impaired by rapid dimerization
AUTHOR(S): Bass, Joseph; Chiu, Gavin; Argon, Yair; Steiner, Donald F.
CORPORATE SOURCE: The Department of Medicine, The University of Chicago, Chicago, IL, 60637, USA
SOURCE: J. Cell Biol. (1998), 141(3), 637-646
CODEN: JCLBA3; ISSN: 0021-9525
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Many complex membrane proteins undergo subunit folding and assembly in the ER before transport to the cell surface. Receptors for insulin and insulin-like **growth** factor I, both integral membrane proteins and members of the family of receptor tyrosine kinases (RTKs), are unusual in that they require homodimerization before export from the ER. To better understand chaperone mechanisms in endogenous membrane protein assembly in living cells, the authors have examd. the folding, assembly, and transport of the human insulin receptor (HIR), a dimeric RTK. Using pulse-chase labeling and nonreducing SDS-PAGE anal., the authors have explored the mol. basis of several sequential maturation steps during receptor biosynthesis. Under normal **growth** conditions, newly synthesized receptor monomers undergo disulfide bond formation while assocd. with the homologous chaperones calnexin (Cnx) and **calreticulin** (Crt). An **inhibitor** of glucose trimming, castanospermine (CST), abolished binding to Cnx/Crt but also unexpectedly accelerated receptor homodimerization resulting in misfolded oligomeric proreceptors whose processing was delayed and cell surface expression was also decreased by .apprx.30%. Prematurely-dimerized receptors were retained in the ER and more avidly assocd. with the heat shock protein of 70 kDa homolog binding protein. In CST-**treated** cells, receptor

misfolding followed disordered oligomerization. Together, these studies demonstrate a chaperone function for Cnx/Crt in HIR folding in vivo and also provide evidence that folding efficiency and homodimerization are counter-balanced.

L4 ANSWER 34 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:192728 HCAPLUS
DOCUMENT NUMBER: 128:292412
TITLE: Standardized characterization of gene expression in human colorectal epithelium by two-dimensional electrophoresis
AUTHOR(S): Reymond, Marc A.; Sanchez, Jean Charles; Hughes, Graham J.; Guenther, Klaus; Riese, Jutta; Tortola, Silvia; Peinado, Miguel A.; Kirchner, Thomas; Hohenberger, Werner; Hochstrasser, Denis F.; Koeckerling, Ferdinand
CORPORATE SOURCE: Dep. Surgery Pathology, Univ. Erlangen, Erlangen, D-91023, Germany
SOURCE: Electrophoresis (1997), 18(15), 2842-2848
CODEN: ELCTDN; ISSN: 0173-0835
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB New diagnostic and prognostic markers are needed in colorectal **cancer**. They can be found by differential anal. at DNA, RNA, or protein level. The accuracy of phenotypic comparisons of **tumor** and normal tissues depends on the purity of the samples. An effective method is presented to identify and isolate proteins that are differentially expressed under altered conditions, and a two-dimensional ref. protein map of the normal human colonic epithelium. Normal colonic mucosa, primary **tumors**, and liver metastases were prepd. in the operating room. After washing in an ice-cold medium contg. protease **inhibitors**, crypts were isolated by mech. prepn. without using metalloproteinases. Epithelial cells were then selected using Ber-EP4 Dynabeads. The samples were denaturated before processing for immobilized pH gradient two-dimensional polyacrylamide gel electrophoresis according to SWISS-2DPAGE stds. The samples contained more than 95% epithelial cells as confirmed by fluorescence-activated cell sorting using pan-anticytokeratin antibodies. Cell surfaces were not damaged, as assessed by scanning electronic microscope. A protein ref. map of the normal colonic epithelium was defined. Using gel matching, N-terminal sequencing and/or immunoblotting techniques, 60 polypeptides - including proteins specifically expressed in colorectal epithelium - have now been identified. This reproducible method of sample prepn. permits the comparison of protein patterns found in various pathol. states with the present ref. map (http://www.expasy.ch). Some of these patterns might provide diagnostic or prognostic markers, or even mol. targets for therapy in the future.

L4 ANSWER 35 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:192727 HCAPLUS
DOCUMENT NUMBER: 128:203697
TITLE: Protein expression profiles in human breast ductal carcinoma and histologically normal tissue

AUTHOR(S): Bini, Luca; Magi, Barbara; Marzocchi, Barbara; Arcuri, Felice; Tripodi, Sergio; Cintorino, Marcella; Sanchez, Jean Charles; Frutiger, Severine; Hughes, Graham; Pallini, Vitaliano; Hochstrasser, Denis F.; Tosi, Piero
CORPORATE SOURCE: Dep. Molecular Biology, Univ. Siena, Siena, I-53100, Italy
SOURCE: Electrophoresis (1997), 18(15), 2832-2841
CODEN: ELCTDN; ISSN: 0173-0835
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ref. two-dimensional (2-D) gels are presented for human breast ductal **carcinoma** and histol. normal tissue. Whole biopsy fragments were analyzed, including epithelial and nonepithelial components. Thirty-five spots have been assigned by gel matching to the human liver SWISS-2DPAGE ref. map and/or to the human primary keratinocyte IPG map from the Danish Center for Human Genome. N-terminal microsequencing was applied to confirm randomly chosen matching assignments and to identify 6 new spots. Protein expression profiles in ductal **carcinoma** and in normal breast tissue appeared to be similar, except for a pattern consisting of 32 spots, which were highly expressed in all **carcinoma** specimens, and less intense and occasionally undetectable in normal tissue. This difference was statistically significant. Assignment has been obtained for several spots, namely GRP94, GRP78, GRP75, mitochondrial HSP60, **calreticulin**, protein disulfide isomerase, peptidyl-prolyl cis-trans isomerase, collagen-binding protein 2, fructose bisphosphate aldolase, glyceraldehyde-3-phosphate dehydrogenase, thioredoxin, cytochrome c oxidase VA subunit, tubulin .beta. isoform, and macrophage migration **inhibitory** factor (MIF). The **cancer**- and tissue-specificity of the described pattern was assessed by matching to the Swiss-2DPAGE human liver, hepatoma, **lymphoma**, erythroleukemia ref. maps. The pattern of 32 spots was found to be indicative of epithelial neoplasia.

L4 ANSWER 36 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:138187 HCAPLUS
DOCUMENT NUMBER: 128:267996
TITLE: Genetic tailoring of N-linked oligosaccharides: the role of glucose residues in glycoprotein processing of Saccharomyces cerevisiae in vivo
AUTHOR(S): Jakob, Claude A.; Burda, Patricie; Te Heesen, Stephan; Aebi, Markus; Roth, Jurgen
CORPORATE SOURCE: Division of Cell and Molecular Pathology, Zurich, CH-8091, Switz.
SOURCE: Glycobiology (1998), 8(2), 155-164
CODEN: GLYCE3; ISSN: 0959-6658
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In higher eukaryotes a quality control system monitoring the folding state of glycoproteins is located in the ER and is composed of the proteins calnexin, **calreticulin**, glucosidase II, and UDP-glucose:glycoprotein glucosyltransferase. It is believed that the

innermost glucose residue of the N-linked oligosaccharide of a glycoprotein serves as a tag in this control system and therefore performs an important function in the protein folding pathway. To address this function, we constructed Saccharomyces cerevisiae strains which contain non-glucosylated (G0), monoglucosylated (G1), or diglucosylated (G2) glycoproteins in the ER and used these strains to study the role of glucose residues in the ER processing of glycoproteins. These alterations of the oligosaccharide structure did not result in a **growth** phenotype, but the induction of the unfolded protein response upon **treatment** with DTT was much higher in G0 and G2 strains as compared to wild-type and G1 strains. Our results provide in vivo evidence that the G1 oligosaccharide is an active oligosaccharide structure in the ER glycoprotein processing pathway of S. cerevisiae. Furthermore, by analyzing N-linked oligosaccharides of the constructed strains we can directly show that no general glycoprotein glucosyltransferase exists in S. cerevisiae.

L4 ANSWER 37 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:85569 HCAPLUS
DOCUMENT NUMBER: 128:202851
TITLE: Cell wall 1,6-.beta.-glucan synthesis in Saccharomyces cerevisiae depends on ER glucosidases I and II, and the molecular chaperone BiP/Kar2p
AUTHOR(S): Simons, Jan Fredrik; Ebersold, Melanie; Helenius, Ari
CORPORATE SOURCE: Department of Cell Biology, Yale University School of Medicine, New Haven, CT, 06520-8002, USA
SOURCE: EMBO J. (1998), 17(2), 396-405
CODEN: EMJODG; ISSN: 0261-4189
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of glucose trimming in the endoplasmic reticulum of Saccharomyces cerevisiae was investigated using glucosidase **inhibitors** and mutant strains devoid of glucosidases I and II. These glucosidases are responsible for removing glucose residues from the N-linked core oligosaccharides attached to newly synthesized polypeptide chains. In mammalian cells they participate together with calnexin, **calreticulin** and UDP-glucose:glycoprotein glucosyltransferase in the folding and quality control of newly synthesized glycoproteins. In S. cerevisiae, glucosidase II is encoded by the GLS2 gene, and glucosidase I, as suggested here, by the CWH41 gene. Using castanospermine (an .alpha.-glucosidase **inhibitor**) and yeast strains defective in glucosidase I, glucosidase II and BiP/Kar2p, it was demonstrated that cell wall synthesis depends on the two glucosidases and BiP/Kar2p. In double mutants with defects in both BiP/Kar2p and either of the glucosidases, the phenotype was particularly clear. Synthesis of 1,6-.beta.-glucan--a cell wall component-was reduced; the cell wall displayed abnormal morphol.; the cells aggregated; and their **growth** was severely **inhibited**. No defects in protein folding or secretion could be detected. It is concluded that glucose trimming in S. cerevisiae is necessary for proper cell wall synthesis, and that the glucosidases function synergistically with BiP/Kar2p in this process.

L4 ANSWER 38 OF 51 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:49834 HCAPLUS
DOCUMENT NUMBER: 126:127307
TITLE: Modulation of the retinoic acid and retinoid X receptor signaling pathways in P19 embryonal carcinoma cells by **calreticulin**
AUTHOR(S): Shago, Mary; Flock, Grace; Leung Hagesteijn, Chung-Yee; Woodside, Michael; Grinstein, Sergio; Giguere, Vincent; Dedhar, Shoukat
CORPORATE SOURCE: Mol. Oncol. Group, Royal Hospital, Montreal, PQ, H3A 1A1, Can.
SOURCE: Exp. Cell Res. (1997), 230(1), 50-60
CODEN: ECREAL; ISSN: 0014-4827
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Calreticulin** is a widely expressed calcium binding protein that can be bind to an amino acid sequence motif, KXGFFKR, which is present in the cytoplasmic domain of all integrin .alpha.-subunits. Closely related sequences, KXFFKR and KXFFRR, are encoded in the DNA-binding domain of all members of the steroid/thyroid/retinoid receptor superfamily and it has recently been demonstrated that **calreticulin inhibits** their activity both in vitro and in vivo. Here we present novel evidence that **calreticulin** can interfere directly with the retinoic acid (RARs) and retinoid X (RXRs) receptor pathways. **Calreticulin** exhibits the ability to **inhibit** DNA-binding activity of both heterodimeric RAR/RXR and homodimeric RXR complexes in vitro. **Inhibition** of RXR binding to DNA is achieved with a concn. of **calreticulin** that is approx. fourfold lower than that required for **inhibition** of RAR/RXR binding to a cognate binding site. Copptn. expts. suggest a direct protein:protein interaction between **calreticulin** and retinoid receptors. Stable overexpression of **calreticulin** in P19 embryonal **carcinoma** cell significantly decreases the rapid activation of the endogenous RA-responsive RAR.beta. gene, abrogates the ability of endogenous RAR/RXR complexes to bind to DNA, and **inhibits** the emergence of the RA-induced differentiated phenotype. These data demonstrate that **calreticulin** can interfere with the two distinct retinoid signaling pathways through a mechanism likely involving direct protein:protein interactions and that disruption of the retinoid signal alters biol. process in vivo.

L4 ANSWER 39 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:48815 HCAPLUS
DOCUMENT NUMBER: 126:65443
TITLE: Method of inhibiting restenosis using **calreticulin**
INVENTOR(S): Michalak, Marek; Lucas, Alexandra
PATENT ASSIGNEE(S): University of Alberta, Can.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9636643	A1	19961121	WO 1996-IB471	19960517
W: AU, CA, JP, MX				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9655120	A1	19961129	AU 1996-55120	19960517
PRIORITY APPLN. INFO.:			US 1995-442844	19950517
			US 1996-649417	19960516
			WO 1996-IB471	19960517

AB This invention relates to **calreticulin**, segments and derivs. thereof and to therapeutic compns. contg. such products for **treating** restenosis. It relates also to methods of producing the products by chem. synthesis or employing recombinant techniques. The invention is also concerned with the use of the products for **treating** patients to **prevent** atherosclerosis development as well as recurrent plaque **growth**. A method of **treating** a patient to **inhibit** restenosis comprises administering to such patient in an amt. which is effective to **inhibit** restenosis a compd. selected from the group consisting of **calreticulin**; the C-domain of **calreticulin**; a C-domain contg. segment of **calreticulin**; and a polypeptide which contains from about 6 to 100 amino acid residues and is an addn., substitution or deletion analog of the C-domain of **calreticulin** having the same functional activity. In a specific embodiment, the polypeptide has the amino acid sequence KEEEEKKRKEEEEAEEDEEDKDDKEDEDEDEEDKDEEEEE.

IT **144713-90-6P**, **Calreticulin** (human)
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; method of inhibiting restenosis using **calreticulin**)

L4 ANSWER 40 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:647919 HCAPLUS
DOCUMENT NUMBER: 125:294014
TITLE: Identification by subtractive hybridization of a spectrum of novel and unexpected genes associated with in vitro differentiation of human cytotrophoblast cells
AUTHOR(S): Morrish, D. W.; Linetsky, E.; Bhardwaj, D.; Li, H.; Dakour, J.; Marsh, R. G.; Paterson, M. C.; Godbout, R.
CORPORATE SOURCE: Department Medicine, University Alberta, Edmonton, AB, T6G 2S2, Can.
SOURCE: Placenta (1996), 17(7), 431-441
CODEN: PLACDF; ISSN: 0143-4004
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have previously demonstrated that epidermal **growth** factor (EGF), colony stimulating factor-1 (CSF-1), and granulocyte-monocyte colony stimulating factor (GMCSF) stimulate, while transforming **growth** factor .beta.1 (TGF.beta.1) **inhibits**, cytotrophoblast differentiation. To identify genes mediating EGF-induced differentiation, we constructed a subtracted cDNA library between

undifferentiated cytotrophoblast and differentiating cytotrophoblast. We identified six novel genes and four known syncytial products .alpha.-human chorionic gonadotrophin (.alpha.hCG) pregnancy-specific .beta.1-glycoprotein, 3.beta.-hydroxysteroid dehydrogenase, and plasminogen activator **inhibitor** type 1 whose mRNAs increased during differentiation. Ten other genes were identified whose mRNAs increased during differentiation. Five of these (keratin 19, **calreticulin**, heat shock protein 27, serum and glucocorticoid-regulated kinase and adrenomedullin) were not previously reported to be expressed in placenta. Five other genes known to be expressed in placenta were identified: keratin 8, fibronectin, mitochondrial ATP synthase, H19, and cytosolic copper-zinc superoxide dismutase (SOD-1). Several of these genes may have regulatory functions in trophoblast differentiation.

L4 ANSWER 41 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:592346 HCAPLUS
DOCUMENT NUMBER: 125:271704
TITLE: Geranylgeraniol causes a decrease in levels of **calreticulin** and tyrosine phosphorylation of a 36-kDa protein prior to the appearance of apoptotic features in HL-60 cells
AUTHOR(S): Nakajo, Shigeo; Okamoto, Mitsuru; Masuda, Yutaka; Sakai, Itaru; Ohsawa, Shigemitsu; Nakaya, Kazuyasu
CORPORATE SOURCE: Lab. Biological Chem., Sch. Pharmaceutical Sci., Showa Univ., Tokyo, 142, Japan
SOURCE: Biochem. Biophys. Res. Commun. (1996), 226(3), 741-745
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It was demonstrated recently that geranylgeraniol (GGO) has potent apoptosis-inducing activity in various lines of **tumor** cells, including HL-60 cells. In the present study, the authors found that GGO markedly **inhibited** the expression of a Ca2+-binding protein, **calreticulin**, prior to the induction of apoptosis in HL-60 cells. Furthermore, they also obsd. a significant decrease in the tyrosine phosphorylation of a 36-kDa protein that is a major tyrosine-phosphorylated protein in HL-60 cells. These findings suggested that decreases in levels of **calreticulin** and in the tyrosine phosphorylation of the 36-kDa protein might be assocd. with the induction of apoptosis by GGO in HL-60 cells.

L4 ANSWER 42 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:580376 HCAPLUS
DOCUMENT NUMBER: 125:204501
TITLE: Use of **calreticulin** in modulating hormone responsiveness and new pharmaceuticals for **treating cancer**, osteoporosis and chronic inflammatory disease
INVENTOR(S): Dedhar, Shoukat
PATENT ASSIGNEE(S): Can.
SOURCE: Can. Pat. Appl., 42 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2140814	AA	19960724	CA 1995-2140814	19950123

AB This invention relates to isolated and purified proteins, such as **calreticulin** and mimetics of **calreticulin**, for a novel use of modulating hormone responsiveness. These proteins are useful in gene therapy and in manufg. pharmaceuticals for **treating** a variety of diseases, including **cancer**, osteoporosis and chronic inflammatory disease. The proteins include or bind to an amino acid sequence KXFFYR, wherein X is either G, A or V and Y is either K or R. This sequence is present in the DNA-binding domain, and is crit. for the DNA binding activity, of a variety of hormone receptors, including glucocorticoid receptor, mineralocorticoid receptor, androgen receptor, progesterone receptor, estrogen receptor, retinoic acid receptor, thyroid hormone receptor and vitamin D receptor. Proteins which bind to this sequence may **inhibit** hormone receptor-induced gene transcription. Proteins which include this sequence may promote hormone receptor-induced gene transcription. The invention includes isolated DNA mols. for these proteins, methods of **treating** diseases using these proteins, synthetic peptides and their mimetics, and kits contg. these proteins, synthetic peptides or their mimetics. **Calreticulin** was found to be present in cell nuclei. Both in vitro and in vivo, **calreticulin inhibited** hormone receptor-hormone responsive element interaction and hormone-induced gene transcription while KXFFYR peptides antagonized this **inhibition**.

L4 ANSWER 43 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:569705 HCAPLUS
DOCUMENT NUMBER: 125:204500
TITLE: **Calreticulin, calreticulin** mimics, and peptide inhibitors of **calreticulin** as modulators of hormone responsiveness and pharmaceuticals
INVENTOR(S): Dedhar, Shoukat; St-Arnaud, Rene
PATENT ASSIGNEE(S): Can.
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9623001	A1	19960801	WO 1995-CA664	19951123

W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE,

IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 5854202	A	19981229	US 1995-377432	19950124
AU 9539203	A1	19960814	AU 1995-39203	19951123
EP 807121	A1	19971119	EP 1995-936911	19951123
R: DE, DK, ES, FR, GB, IT, NL				
JP 2000507801	T2	20000627	JP 1996-522508	19951123
AU 9945861	A1	19991028	AU 1999-45861	19990901

PRIORITY APPLN. INFO.:

US 1995-377432	A2	19950124
AU 1995-39203	A3	19951123
WO 1995-CA664	W	19951123

AB This invention relates to isolated and purified proteins, such as **calreticulin** and mimetics and **inhibitors** of **calreticulin**, for use in modulating hormone responsiveness. These proteins are useful in gene therapy and in manufg. pharmaceuticals for **treating** a variety of diseases, including **cancer**, osteoporosis and chronic inflammatory disease. The proteins include or bind to an amino acid sequence KXFFYR (X = G, A, V; Y = K, R). This sequence is present in the DNA-binding domain, and is crit. for the DNA binding activity, of a variety of hormone receptors, including glucocorticoid receptor, mineralocorticoid receptor, androgen receptor, progesterone receptor, estrogen receptor, retinoic acid receptor, thyroid hormone receptor and vitamin D receptor. Proteins which bind to this sequence may **inhibit** hormone receptor-induced gene transcription. Proteins which include this sequence may promote hormone receptor-induced gene transcription. The invention includes isolated DNA mols. for these proteins, methods of **treating** diseases using these proteins, synthetic peptides and their mimetics, and kits contg. these proteins, synthetic peptides or their mimetics. **Calreticulin** was visualized in cell nuclei. Recombinant **calreticulin inhibited** binding of androgen receptor to its response element. Neuronal differentiation of P19EC cells was **inhibited** by increased levels of **calreticulin** but enhanced by decreased levels of **calreticulin**. **Calreticulin** overexpression in osteoblastic cell line MC3T3-E1 also **inhibited** vitamin D-induced stimulation of calcium incorporation into the extracellular matrix.

L4 ANSWER 44 OF 51 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:	1996:381588 HCAPLUS
DOCUMENT NUMBER:	125:110917
TITLE:	**Inhibition** of retinoic acid receptor function and retinoic acid-regulated gene expression in mouse **melanoma** cells by **calreticulin**. A potential pathway for cyclic AMP regulation of retinoid action
AUTHOR(S):	Desai, Dinakar; Michalak, Marek; Singh, Nishi K.; Niles, Richard M.
CORPORATE SOURCE:	Department Biochemistry Molecular Biology, Marshall University School Medicine, Huntington, WV, 25755, USA
SOURCE:	J. Biol. Chem. (1996), 271(25), 15153-15159 CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Calcium is a second messenger that controls a wide variety of cellular functions. Because of its multiple actions, there is a stringent requirement for calcium homeostasis, and this is achieved in part by a system of transport and storage proteins such as **calreticulin** located in the endoplasmic reticulum. **Calreticulin** is also found in the nucleus, suggesting that it may have a role in transcriptional regulation. It has been reported that **calreticulin** can **inhibit** steroid-regulated gene transcription by **preventing** receptor binding to DNA. Here we report that overexpression of the **calreticulin** gene in B16 mouse **melanoma** cells resulted in a decrease in retinoic acid (RA)-stimulated reporter gene expression. Gel shift anal. showed that purified **calreticulin inhibited** the binding of endogenous RAR to a .beta.-RA response element oligonucleotide, only if added prior the addn. of the oligonucleotide. Co-immunopptn. studies suggest a phys. interaction between RAR and **calreticulin**. Transfection of the **calreticulin** gene into B16 cells **inhibited** the RA induction of protein kinase C.alpha., a marker of RA-induced differentiation. We also found that cAMP increased the expression of **calreticulin**. CAMP may act to antagonize RA action by both decreasing RAR expression and stimulating **calreticulin** levels.

L4 ANSWER 45 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:245004 HCAPLUS
DOCUMENT NUMBER: 125:183
TITLE: Control of tumor progression by maintenance of apoptosis
AUTHOR(S): Bruchovsky, Nicholas; Snoek, Rob; Rennie, Paul S.; Akakura, Koichiro; Goldenberg, S. Larry; Gleave, Martin
CORPORATE SOURCE: Department Cancer Endocrinology, BC Cancer Agency, Vancouver, BC, V5Z 4E6, Can.
SOURCE: Prostate (N. Y.) (1996), (Suppl. 6), 13-21
CODEN: PRSTDS; ISSN: 0270-4137
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review, with 27 refs. The ability to induce multiple apoptotic regressions of an androgen-dependent **tumor** cell population by repeated cycles of androgen withdrawal and replacement may be advantageous in therapeutic strategies aimed at delaying or **preventing** **tumor** progression. With greater insight into factors that either initiate or limit apoptosis, more efficient application of intermittent therapy might be achieved, esp. if methods could be devised to increase the length or no. of **treatment** cycles. Both **calreticulin** and clusterin represent proteins with a potential role in the regulation of apoptosis. **Calreticulin** may **inhibit** target gene transcription by interacting with steroid hormone receptors, thereby masking their DNA-binding sites and triggering the onset of the apoptotic process. Clusterin, on the other hand, is a membrane-stabilizing protein that appears to be involved in limiting the autophagic lysis of epithelial cells during apoptosis. Also, the increasing tendency for nuclear localization of clusterin after androgen withdrawal may preserve the nuclear environment, limiting the lethal

effect of **treatment**. Thus, **tumor** progression, characterized by the loss of apoptotic potential, appears to be linked in part to the inappropriate activation of the TRPM-2 gene, which accounts for the constitutive expression of clusterin.

L4 ANSWER 46 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:175690 HCAPLUS
DOCUMENT NUMBER: 124:220506
TITLE: Inositol triphosphate receptors as targets for treating cell proliferative disorders by modulating signal transduction
INVENTOR(S): Fischer, Gabriela A.; Ullrich, Axel
PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V., Germany
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9600586	A2	19960111	WO 1995-EP2532	19950629
WO 9600586	A3	19960215		
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9529789	A1	19960125	AU 1995-29789	19950629
PRIORITY APPLN. INFO.:			US 1994-268390	19940630
			WO 1995-EP2532	19950629

AB The present invention relates to the use of proteins, peptides and org. mols. capable of modulating inositol 1,4,5-triphosphate (IP3) receptor signal transduction in order to **inhibit** or reverse inappropriate **growth** of cells assocd. with abnormalities of signal transduction assocd. with tyrosine kinases. The present invention also relates to the use of IP3 receptor mutants in the **treatment** of proliferative disorders assocd. with abnormalities of signal transduction assocd. with tyrosine kinases, including **cancer**. The present invention also relates to the use of IP3 receptor and genetically engineered host cells that express the IP3 receptor to evaluate and screen for substances and compds. that modulate IP3 receptor activities.

L4 ANSWER 47 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:796651 HCAPLUS
DOCUMENT NUMBER: 123:189325
TITLE: Components of the protein synthesis and folding machinery are induced in vascular smooth muscle cells by hypertrophic and hyperplastic agents. Identification by comparative protein phenotyping and

microsequencing
AUTHOR(S): Patton, Wayne F.; Erdjument-Bromage, Hediye; Marks, Andrew R.; Tempst, Paul; Taubman, Mark B.
CORPORATE SOURCE: Mol. Biol. Program, Memorial Sloan-Kettering Cancer Cent., New York, NY, 10021, USA
SOURCE: J. Biol. Chem. (1995), 270(36), 21404-10
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Vascular smooth muscle cells (VSMC) are the principal cellular component of the blood vessel wall. Atherosclerosis, hypertension, and **angiogenesis** are assocd. with abnormal VSMC **growth**. Angiotensin II is hypertrophic for cultured adult rat aortic VSMC, whereas platelet-derived **growth** factor and serum are hyperplastic. To identify changes in specific proteins assocd. with either hyperplastic or hypertrophic **growth**, high resoln. two-dimensional gel electrophoresis was performed on exts. from quiescent rat aortic VSMC and from VSMC exposed for 24 h to **growth** factors (10% fetal calf serum, platelet-derived **growth** factor, or angiotensin II). Twelve proteins were up-regulated and 5 down-regulated by **treatment** with **growth** factors. Eight of the up-regulated and one of the down-regulated proteins were identified by internal protein microsequencing from electroblotted two-dimensional gels or by co-electrophoresis of purified proteins in two-dimensional gels. Four of the proteins up-regulated by **growth** factors were identified as mediators of protein folding. These were heat shock proteins, HSP-60 and HSP-70, protein disulfide isomerase, and protein disulfide isomerase isoenzyme Q-2. Addnl. proteins were identified as elongation factor EF-1.beta., a component of the protein synthesis app., and **calreticulin**, another putative mol. chaperone. Vimentin and actin were also upregulated, whereas an isoform of myosin heavy chain was down-regulated. Hyperplastic and hypertrophic **growth** were accompanied by similar changes in protein expression, suggesting that both types of **growth** require up-regulation of the protein synthesis and folding machinery.

L4 ANSWER 48 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:688145 HCAPLUS
DOCUMENT NUMBER: 123:78641
TITLE: Enhanced expression of **calreticulin** in the nucleus of radioresistant squamous carcinoma cells in response to ionizing radiation
AUTHOR(S): Ramsamooj, Priya; Notario, Vicente; Dritschilo, Anatoly
CORPORATE SOURCE: Dep. of Radiation Medicine, Georgetown Univ. Med. Center, Washington, DC, 20007, USA
SOURCE: Cancer Res. (1995), 55(14), 3016-21
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ionizing radiation has been shown to modulate gene and protein expression as well as cellular signal transduction pathways. However, the biochem. and mol. mechanisms that underlie the cellular response to radiation are not fully understood. The effects of ionizing radiation on the expression

of nuclear proteins have now been investigated in radioresistant human head and neck squamous **carcinomas** cells (SQ-20B cells) using the techniques of two-dimensional PAGE, silver staining, and computer-assisted quant. anal. .gamma.-Radiation (600 cGy) induced the expression of 10 proteins and suppressed the expression of 5 proteins in the nuclei of SQ-20B cells as detected 4 h after **treatment**. Electroelution and NH2-terminal amino acid sequence anal. revealed that one of the radiation-induced proteins was the Ca2+-binding protein **calreticulin**. The expression of **calreticulin** was increased approx. 6-fold in the nuclei of irradiated SQ-20B cells. **Calreticulin** and the other proteins whose expression was affected by radiation may contribute to the radioresistance phenotype of SQ-20B cells.

L4 ANSWER 49 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:685391 HCAPLUS
DOCUMENT NUMBER: 123:140514
TITLE: Cell surface **calreticulin** is a putative mannoside lectin which triggers mouse melanoma cell spreading
AUTHOR(S): White, Tracy K.; Zhu, Qiang; Tanzer, Marvin L.
CORPORATE SOURCE: Dep. BioStructure and Function, Univ. Connecticut Health Center, Farmington, CT, 06030-3705, USA
SOURCE: J. Biol. Chem. (1995), 270(27), 15926-9
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB B16 mouse **melanoma** cells adhere to and spread on laminin. We have previously shown that cell preading is uncoupled from adhesion when unglycosylated laminin is used as a substratum; spreading was restored by a Pronase digest of laminin which became inactive when it was specifically depleted of its mannoside peptides; spreading was also specifically restored by mannosides such as mannan, Man9, and Man6, but not Man3. The effector mannosides bind to a cell surface receptor, previously shown by direct and indirect methods. We have now identified the receptor as cell surface **calreticulin** by isolating it via mannan affinity chromatog. and showing its sequence identity with mouse **calreticulin**. Anti-**calreticulin** antibodies confirm this identity, decorate the B16 cell surface, and block cell spreading. Purified B16 cell **calreticulin** from whole cell lysates successfully competes with cell surface **calreticulin** and **prevents** cell spreading. The composite data implicate cell surface **calreticulin** as a putative lectin that must be occupied to initiate spreading of laminin-adherent B16 cells.

L4 ANSWER 50 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:500297 HCAPLUS
DOCUMENT NUMBER: 122:255933
TITLE: **Calreticulin**, an antithrombotic agent which binds to vitamin K-dependent coagulation factors, stimulates endothelial nitric oxide production, and limits thrombosis in canine coronary arteries
AUTHOR(S): Kuwabara, Keisuke; Pinsky, David J.; Schmidt, Ann Marie; Benedict, Claude; Brett, Jerold; Ogawa,

Satoshi; Broekman, M. Johan; Marcus, Aaron J.; Sciacca, Robert R.; et al.
CORPORATE SOURCE: Coll. Physicians and Surgeons, Columbia Univ., New York, NY, 10032, USA
SOURCE: J. Biol. Chem. (1995), 270(14), 8179-87
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Coagulation Factor IX/IXa has been shown to bind to cellular surfaces, and Factor IXa expresses its procoagulant activity by assembling into the intrinsic Factor X activating complex (Factors IXa/VIIIa/X), which also forms on membrane surfaces. This led us to identify cellular proteins which bind Factor IX/IXa; an .apprxeq.55-kDa polypeptide was purified to homogeneity from bovine lung exts. based on its capacity to bind 125I-Factor IX in a dose-dependent and saturable manner. From protein sequence data of the amino terminus and internal peptides, the .apprxeq.55-kDa polypeptide was identified as **calreticulin**, a previously identified intracellular calcium-binding protein. Recombinant **calreticulin** bound vitamin K-dependent coagulation factors, 125I-Factor IX, 125I-Factor X, and 125I-prothrombin (Kd values of .apprxeq.2.7, 3.2, and 8.3 nM, resp.), via interaction with its C-domain, although it did not affect the coagulant properties of these proteins. 125I-**Calreticulin** also bound to **endothelial** cells in vitro (Kd .apprxeq. 7.4 nM), and mouse infusion studies showed an initial rapid phase of clearance in which **calreticulin** could be localized on the vascular **endothelium**. Exposure of **endothelial** cells to **calreticulin** led to dose-dependent, immediate, and sustained increase in the prodn. of nitric oxide, as measured using a porphyrinic microsensor. In a canine elec. induced thrombosis model, intracoronary infusion of **calreticulin** (n = 7) **prevented** occlusion of the left circumflex coronary artery in a dose-dependent manner compared with vehicle-**treated** controls (n = 5). These results indicate that **calreticulin** interacts with the **endothelium** to stimulate release of nitric oxide and **inhibit** clot formation.

L4 ANSWER 51 OF 51 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:629264 HCAPLUS
DOCUMENT NUMBER: 115:229264
TITLE: Regulation of expression and intracellular distribution of **calreticulin**, a major calcium binding protein of nonmuscle cells
AUTHOR(S): Opas, Michal; Dziak, Ewa; Fliegel, Larry; Michalak, Marek
CORPORATE SOURCE: Dep. Anat., Univ. Toronto, Toronto, ON, M5S 1A8, Can.
SOURCE: J. Cell. Physiol. (1991), 149(1), 160-71
CODEN: JCLLAX; ISSN: 0021-9541
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the present study the presence was demonstrated of **calreticulin**, a major Ca2+-sequestering protein of nonmuscle cells, in a variety of cell types in tissue culture. The protein localizes to the endoplasmic reticulum in most cell types and also to the nuclear envelope or nucleoli-like structures in some cell types. **Calreticulin** is

enriched in the rough endoplasmic reticulum, suggesting a possible involvement in protein synthesis. **Calreticulin** terminates with the KDEL-COOH sequence, which is likely responsible for its endoplasmic reticulum localization. Unlike some other KDEL proteins, **calreticulin** expression is neither heat-shock nor Ca2+-shock dependent. Using a variety of metabolic **inhibitors**, it was shown that the pool of **calreticulin** in L6 cells has a relatively slow turnover and a stable intracellular distribution. In proliferating muscle cells in culture (both L6 and human skeletal muscle) **calreticulin** is present in the endoplasmic reticulum, and addnl. intranuclear staining is obsd. When fusion of the L6 cells is **inhibited** with either a high serum concn. or transforming **growth** factor .beta. or TPA, the nucleolar staining by **anticalreticulin** antibodies is diminished, although the presence of **calreticulin** in the endoplasmic reticulum remains unchanged. In contrast, in differentiated (i.e., fused) muscle cells neither intranuclear nor intracellular staining for **calreticulin** is present. Evidently, **calreticulin** is abundant in the endoplasmic reticulum in proliferating myoblasts, while it is present in only small amts. in sarcoplasmic reticulum membranes in terminally differentiated myotubes. A model is proposed for the domain structure of **calreticulin** that may explain the differential subcellular distribution of this protein. Because of its widespread distribution in nonmuscle tissues, it is postulated that **calreticulin** is a multifunctional protein that plays an important role in Ca2+ sequestering and thus that it is the nonmuscle analog of calsequestrin.

09/807,148 Search notes

Set	Items	Description
S1	2106	CALRETICULIN?
S2	2741009	CANCER? OR TUMOR?
S3	281	S1 AND S2
S4	29	S3 AND (ANGIO? OR ENDOTHEL?)
S5	14	RD (unique items)

5/9/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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13869166 BIOSIS NO.: 200200497987
A gene therapy for cancer **based on the** angiogenesis **inhibitor, vasostatin.**
AUTHOR: Xiao F; Wei Y(a); Yang L; Zhao X; Tian L; Ding Z; Yuan S; Lou Y; Liu F; Wen Y; Li J; Deng H; Kang B; Mao Y; Lei S; He Q; Su J; Lu Y; Niu T ; Hou J; Huang M-J
AUTHOR ADDRESS: (a)Key Laboratory of Biotherapy of Human Diseases and Cancer Center, West China Medical School, West China Hospital, Sichuan University, Guo Xue Xiang, Number 37, Chengdu, Sichuan, 610041**China
JOURNAL: Gene Therapy 9 (18):p1207-1213 September, 2002
MEDIUM: print
ISSN: 0969-7128
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The growth and persistence of solid **tumors** and their metastasis are **angiogenesis** -dependent. Vasostatin, the N-terminal domain of **calreticulin** inclusive of amino acids 1-180, is a potent **angiogenesis** inhibitor. To investigate whether intramuscular administration of vasostatin gene has the anti- **tumor** activity in mouse **tumor** models, we constructed a plasmid DNA encoding vasostatin and a control vector. Production and secretion of vasostatin protein by COS cells transfected with the plasmid DNA encoding vasostatin (pSecTag2B-vaso) were confirmed by Western blot analysis and ELISA. Conditioned medium from vasostatin-transfected COS cells apparently inhibited human umbilical vein **endothelial** cell (HUVEC) and mouse **endothelial** cell (SVEC4-10) proliferation, compared with conditioned medium from the COS cells transfected with control vector or non-transfected cells. Treatment with pSecTag2B-vaso twice weekly for 4 weeks resulted in the inhibition of **tumor** growth and the prolongation of the survival of **tumor** -bearing mice. The sustained high level of vasostatin protein in serum could be identified in ELISA. **Angiogenesis** was apparently inhibited in **tumor** by immunohistochemical analysis. **Angiogenesis** was also inhibited in the chicken embryo CAM assay and mouse corneal micropocket assay. The increased apoptotic cells were found within the **tumor** tissues from the mice treated with plasmid DNA encoding vasostatin. Taken together, the data in the present study indicate that the **cancer** gene therapy by the intramuscular delivery of plasmid DNA encoding vasostatin, is effective in the inhibition of the systemic **angiogenesis** and **tumor** growth in murine models. The present findings also provide further evidence of the anti- **tumor** effects of the vasostatin, and may be of importance for the further exploration of the application of this molecule in the treatment of **cancer** .

REGISTRY NUMBERS: 144638-61-9: VASOSTATIN

5/9/13 (Item 2 from file: 159)
DIALOG(R)File 159:Cancerlit
(c) format only 2002 Dialog Corporation. All rts. reserv.

02233143 PMID: 96649366
Second annual CaP Cure scientific retreat.
No affiliation given
Non-serial 1995, Second Annual CaP Cure Scientific Retreat (Association for the Cure of Cancer of the Prostate), Santa Barbara, California, September 21-24, 1995.,
Document Type: MONOGRAPH
Languages: ENGLISH
Main Citation Owner: NOTNLM

Record type: Completed

The Second Annual CaP Cure (Association for the Cure of **Cancer** of the Prostate) Scientific Retreat was held September 21-24, 1995 in Santa Barbara, CA. The retreat consisted of six sessions with the following presentation titles: the challenge of prostate **cancer** ; the enhancement of prostate **cancer** radiosensitivity by androgen withdrawal therapy; mechanisms of radiation-induced cell kill in prostate **cancer** ; isolation and identification of endogenous inhibitors of prostate **cancer** growth and regulation of VEGF and HB-EGF in prostate **cancer** ; prostatic carcinoma therapy with **angiogenin** antagonists; T-cell mediated immunotherapy for prostate **cancer** ; development of a cytokine gene therapy approach to human prostate carcinoma using retroviral vectors carrying two cytokine genes; development of an effective monoclonal antibody based therapy for prostate **cancer** ; a four arm double blind randomized phase Ib trial of bispecific antibody MDX210 vs 520C9Fab 'XP3Fab' vs placebo for treatment of advanced prostate **cancer** expressing HER-2/NEU; bispecific monoclonal antibody immunotherapy of prostate **cancer** ; overview of prostate **cancer** research in Japan; immunotherapy of prostate **cancer** using cytokine gene modified **tumor** vaccines; PSA drive toxic gene(s) for potential treatment of prostate **cancer** ; update of Johns Hopkins experience with GUAX; combination chemotherapy and immunotherapy of metastatic prostate **cancer** ; therapeutic approaches for the treatment of human prostate **cancer** metastasis; combination biological/gene therapy for metastatic prostate **cancer** in a transgenic/mouse prostate model; the biology and therapy of human prostate **cancer** metastasis; a novel approach for gene therapy of prostate **cancer** ; special lecture on **tumor** biology; combination therapy for prostatic **cancer** with chemotherapy and inhibitors of receptor tyrosine kinase mediated signal transduction; strategies for the characterization and therapeutic exploitation of relevant androgen-independent pathways of prostate **cancer** progression; new therapeutic strategies for prostate **cancer** ; update on the FDA's guidelines for new drugs; lipid signaling pathways in hormone-refractory prostate **cancer** cells: an attractive target for new drug development; combined chemohormonal therapy for newly diagnosed metastatic prostate **cancer** ; clinical trials of perillyl alcohol and polyamine analog BE-4-4-4-4 AS anti-prostate **cancer** agents; rational design of suramin analogue anticancer drugs; clinical trial: vitamin D treatment of prostate **cancer** ; loss of functional androgen receptor in androgen independent state prostate **cancer** ; androgen receptor mutations in advanced prostate **cancer** ; **calreticulin** mediated inhibition of androgen receptor activity and prostatic **tumor** cell growth; development of new therapeutic strategies based on genetic alterations in advanced prostate **cancer** ; identification of the molecular determinants of lethal disease in prostate **cancer** : E-cadherin as a marker and a therapeutic agent; identification of a **tumor** suppressor gene for prostate adenocarcinoma on chromosome 16q; identification of a putative **tumor** suppressor gene involved in the progression of prostatic carcinoma; PTI: a new genetic marker in prostate **cancer** ; progression to androgen independence: phase II identification of clinically relevant molecular events; establishment of a prostate **cancer** tissue bank; identification of the hereditary prostate **cancer** (PHC) gene(s); development of a genetics consortium; expression of stimulatory and inhibitory factors in bone which affect metastatic prostate carcinoma; characterization of bone derived growth factors associated with the development of prostate **cancer** metastasis; overview of **tumor** vaccines; development of a PSA based prodrug for androgen independent prostatic **cancer** ; bcl-2 and dysregulation of programmed cell death in prostate **cancer** : opportunities for new therapeutic approaches; death genes, anti-death genes and prostate **cancer** ; molecular regulation and therapeutic induction of apoptotic cell death during prostate **cancer** progression; ev(ABSTRACT TRUNCATED)

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show files
File 155:MEDLINE(R) 1966-2001/Nov W3
File   5:Biosis Previews(R) 1969-2001/Oct W3
         (c) 2001 BIOSIS
File  34:SciSearch(R) Cited Ref Sci 1990-2001/Oct W3
         (c) 2001 Inst for Sci Info
File  35:Dissertation Abs Online 1861-2001/Oct
         (c) 2001 ProQuest Info&Learning
File  71:ELSEVIER BIOBASE 1994-2001/Oct W3
         (c) 2001  Elsevier Science B.V.
File  73:EMBASE 1974-2001/Oct W2
         (c) 2001 Elsevier Science B.V.
File  76:Life Sciences Collection 1982-2001/Oct
         (c) 2001 Cambridge Sci Abs
File 144:Pascal 1973-2001/Oct W3
         (c) 2001 INIST/CNRS
File 149:TGG Health&Wellness DB(SM) 1976-2001/Oct W2
         (c) 2001 The Gale Group
File 172:EMBASE Alert 2001/Oct W3
         (c) 2001 Elsevier Science B.V.
File 342:Derwent Patents Citation Indx 1978-01/200156
         (c) 2001 Derwent Info Ltd
File 345:Inpadoc/Fam.& Legal Stat 1968-2001/UD=200141
         (c) 2001 EPO
File 351:Derwent WPI 1963-2001/UD,UM &UP=200161
         (c) 2001 Derwent Info Ltd
File 357:Derwent Biotechnology Abs 1982-2001/Dec B1
         (c) 2001 Derwent Publ Ltd
File 440:Current Contents Search(R) 1990-2001/Oct W4
         (c) 2001 Inst for Sci Info
?ds

Set     Items   Description
S1        182   CALRETICULIN AND (CANCER? OR CARCIN? OR NEOPLASM? OR TUMOR?
                 OR TUMOUR? OR SARCOM? OR LYMPHOM? OR MELANO? OR LEUKEM? OR A-
                NGIOGEN? OR ENDOTHEL? OR GROWTH)(5N)(INHIBIT? OR PREVENT? OR -
                TREAT?)
S2         61   RD (unique items)
?t2/3 ab/1-61
>>>No matching display code(s) found in file(s): 342, 345

 2/AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11689680   21429266   PMID: 11544272
 Tumor-specific immunity and antiangiogenesis generated by a DNA vaccine
encoding calreticulin linked to a tumor antigen.
  Cheng WF; Hung CF; Chai CY; Hsu KF; He L; Ling M; Wu TC
  Department of Pathology, Johns Hopkins Medical Institutions, Baltimore,
Maryland 21205, USA.
  Journal of clinical investigation (United States)  Sep 2001,  108  (5)
 p669-78,  ISSN 0021-9738   Journal Code: HS7
  Languages: ENGLISH
  Document type: Journal Article
  Record type: Completed
  Antigen-specific cancer immunotherapy and antiangiogenesis have emerged
as two attractive strategies for cancer treatment . An innovative
approach that combines both mechanisms will likely generate the most potent
antitumor effect. We tested this approach using calreticulin (CRT), which
has demonstrated the ability to enhance MHC class I presentation and
exhibit an antiangiogenic effect. We explored the linkage of CRT to a model
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tumor antigen, human papilloma virus type-16 (HPV-16) E7, for the development of a DNA vaccine. We found that C57BL/6 mice vaccinated intradermally with CRT/E7 DNA exhibited a dramatic increase in E7-specific CD8(+) T cell precursors and an impressive antitumor effect against E7-expressing tumors compared with mice vaccinated with wild-type E7 DNA or CRT DNA. Vaccination of CD4/CD8 double-depleted C57BL/6 mice and immunocompromised (BALB/c nu/nu) mice with CRT/E7 DNA or CRT DNA generated significant reduction of lung tumor nodules compared with wild-type E7 DNA, suggesting that antiangiogenesis may have contributed to the antitumor effect. Examination of microvessel density in lung tumor nodules and an in vivo angiogenesis assay further confirmed the antiangiogenic effect generated by CRT/E7 and CRT. Thus, cancer therapy using CRT linked to a tumor antigen holds promise for treating tumors by combining antigen-specific immunotherapy and antiangiogenesis.

2/AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11195382 20532775 PMID: 11080277
Aluminum-induced 1-->3-beta-D-glucan inhibits cell-to-cell trafficking of molecules through plasmodesmata. A new mechanism of aluminum toxicity in plants.

Sivaguru M; Fujiwara T; Samaj J; Baluska F; Yang Z; Osawa H; Maeda T; Mori T; Volkmann D; Matsumoto H

Research Institute for Bioresources, Okayama University, Kurashiki 710-0046, Japan.

Plant physiology (UNITED STATES) Nov 2000, 124 (3) p991-1006, ISSN 0032-0889 Journal Code: P98

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Symplastic intercellular transport in plants is achieved by plasmodesmata (PD). These cytoplasmic channels are well known to interconnect plant cells to facilitate intercellular movement of water, nutrients, and signaling molecules including hormones. However, it is not known whether Al may affect this cell-to-cell transport process, which is a critical feature for roots as organs of nutrient/water uptake. We have microinjected the dye lucifer yellow carbohydrazide into peripheral root cells of an Al-sensitive wheat (Triticum aestivum cv Scout 66) either before or after Al treatment and followed the cell-to-cell dye-coupling through PD. Here we show that the Al-induced root growth inhibition is closely associated with the Al-induced blockage of cell-to-cell dye coupling. Immunofluorescence combined with immuno-electron microscopic techniques using monoclonal antibodies against 1-->3-beta-D-glucan (callose) revealed circumstantial evidence that Al-induced callose deposition at PD may responsible for this blockage of symplastic transport. Use of 2-deoxy-D-glucose, a callose synthesis inhibitor, allowed us to demonstrate that a reduction in callose particles correlated well with the improved dye-coupling and reduced root growth inhibition . While assessing the tissue specificity of this Al effect, comparable responses were obtained from the dye-coupling pattern in tobacco (Nicotiana tabacum) mesophyll cells. Analyses of the Al-induced expression of PD-associated proteins, such as calreticulin and unconventional myosin VIII, showed enhanced fluorescence and co-localizations with callose deposits. These results suggest that Al-signal mediated localized alterations to calcium homeostasis may drive callose formation and PD closure. Our data demonstrate that extracellular Al-induced callose deposition at PD could effectively block symplastic transport and communication in higher plants.

2/AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10596285 20203759 PMID: 10741715
Immunoprotective activities of multiple chaperone proteins isolated from murine B-cell leukemia/lymphoma.
Graner M; Raymond A; Romney D; He L; Whitesell L; Katsanis E
Department of Pediatrics, Steele Memorial Children's Research Center, University of Arizona, Tucson 85724-5073, USA.
Clinical cancer research (UNITED STATES) Mar 2000, 6 (3) p909-15, ISSN 1078-0432 Journal Code: C2H
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Although the use of tumor-derived heat shock/chaperone proteins (HSPs) as anticancer vaccines is gaining wider study and acceptance, there have thus far been no reports concerning chaperone antitumor activities against disseminated hematological malignancies. We have devised an efficient and effective method for purification of the chaperone proteins grp94/gp96, HSP90, HSP70, and calreticulin from harvested A20 murine leukemia/lymphoma tumor material. We have demonstrated that these purified proteins, when used as vaccines, can induce potent and specific immunity against a lethal tumor challenge. Individual chaperone proteins were differentially effective in their abilities to provide immune protection. The increase in survival generated by the most effective chaperone vaccine, HSP70, resulted from at least a 2-log reduction in tumor burden. Syngeneic granulocyte macrophage colony-stimulating factor producing fibroblasts were injected at the site of vaccination in an attempt to augment the immune response. Surprisingly, localized granulocyte macrophage colony-stimulating factor production inhibited the protective effects of chaperone vaccination. These studies provide evidence that chaperone proteins can be isolated from B-cell tumors and used effectively to immunize against disseminated lymphoid malignancies.

2/AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10406128 20002861 PMID: 10529470
KDEL proteins are found on the surface of NG108-15 cells.
Xiao G; Chung TF; Pyun HY; Fine RE; Johnson RJ
Department of Chemistry, Boston University, Boston, MA 02215, USA.
Brain research. Molecular brain research (NETHERLANDS) Oct 1 1999, 72 (2) p121-8, ISSN 0169-328X Journal Code: MBR
Contract/Grant No.: R37AG05894, AG, NIA
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Although KDEL proteins are primarily localized to the endoplasmic reticulum (ER), we have employed surface biotinylation method to demonstrate that the KDEL proteins calreticulin (Crt), protein disulfide isomerase (PDI) and the 78-kDa glucose regulated protein (GRP78) are found on the surface of the NG108-15 cell line. In contrast, the 94-kDa glucose regulated protein (GRP94), another KDEL protein, is not found on the cell surface. Calnexin (Cnx), a type-1 integral transmembrane ER protein which is partially homologous to Crt but lacks the KDEL sequence, is not detected on the cell surface either. While only small amounts of the total GRP78, PDI and Crt molecules exist on the cell surface at steady state, a significant fraction of the newly synthesized molecules are transported to the cell surface and transport of these proteins is inhibited by treatment with brefeldin A. The surface GRP78 contains the KDEL sequence. On the cell

surface, GRP78, PDI and Crt associate with other proteins and form complexes of different sizes. Surface Crt is found to be essential for the neurite formation when NG108-15 cells are induced to differentiate using dibutyryl cAMP.

2/AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10349172 99428332 PMID: 10498619
Calreticulin and calreticulin fragments are endothelial cell inhibitors that suppress tumor growth.
Pike SE; Yao L; Setsuda J; Jones KD; Cherney B; Appella E; Sakaguchi K; Nakhasi H; Atreya CD; Teruya-Feldstein J; Wirth P; Gupta G; Tosato G
Center for Biologics Evaluation, Rockville, MD 20852, USA.
Blood (UNITED STATES) Oct 1 1999, 94 (7) p2461-8, ISSN 0006-4971 Journal Code: A8G
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Several angiogenesis inhibitors are fragments of larger proteins that are themselves not active as angiogenesis inhibitors . Vasostatin, the N-terminal domain of calreticulin inclusive of amino acids 1-180, is an angiogenesis inhibitor that exerts antitumor effects in vivo. In the present study, we examined whether the full-length calreticulin molecule shares the antiangiogenic and antitumor activities of vasostatin. Similar to vasostatin, calreticulin selectively inhibited endothelial cell proliferation in vitro, but not cells of other lineages, and suppressed angiogenesis in vivo. When inoculated into athymic mice, calreticulin inhibited Burkitt tumor growth comparably with vasostatin. Calreticulin lacking the N-terminal 1-120 amino acids inhibited endothelial cell proliferation in vitro and Burkitt tumor growth in vivo comparably with vasostatin. An internal calreticulin fragment encompassing amino acids 120-180 also inhibited endothelial cell proliferation in vitro and angiogenesis in vivo comparably with calreticulin and vasostatin. These results suggest that the antiangiogenic activities of vasostatin reside in a domain that is accessible from the full-length calreticulin molecule and localize to calreticulin N-terminal amino acids 120-180. Thus, calreticulin and calreticulin fragments are inhibitors of angiogenesis that directly target endothelial cells, inhibit angiogenesis , and suppress tumor growth . This information may be critical in designing targeted inhibitors of pathological angiogenesis that underlies cancer and other diseases.

2/AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09996853 99077919 PMID: 9858521
Vasostatin, a calreticulin fragment, inhibits angiogenesis and suppresses tumor growth.
Pike SE; Yao L; Jones KD; Cherney B; Appella E; Sakaguchi K; Nakhasi H; Teruya-Feldstein J; Wirth P; Gupta G; Tosato G
Center for Biologics Evaluation and Research, Rockville, Maryland 20852, USA.
Journal of experimental medicine (UNITED STATES) Dec 21 1998, 188 (12) p2349-56, ISSN 0022-1007 Journal Code: I2V
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

An endothelial cell inhibitor was purified from supernatant of an Epstein-Barr virus-immortalized cell line and identified as fragments of calreticulin . The purified recombinant NH2-terminal domain of calreticulin (amino acids 1-180) inhibited the proliferation of endothelial cells, but not cells of other lineages, and suppressed angiogenesis in vivo. We have named this NH2-terminal domain of calreticulin vasostatin. When inoculated into athymic mice, vasostatin significantly reduced growth of human Burkitt lymphoma and human colon carcinoma . Compared with other inhibitors of angiogenesis , vasostatin is a small, soluble, and stable molecule that is easy to produce and deliver. As an angiogenesis inhibitor that specifically targets proliferating endothelial cells, vasostatin has a unique potential for cancer treatment .

2/AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09719631 98163345 PMID: 9504817
Protein expression profiles in human breast ductal carcinoma and histologically normal tissue.
Bini L; Magi B; Marzocchi B; Arcuri F; Tripodi S; Cintorino M; Sanchez JC ; Frutiger S; Hughes G; Pallini V; Hochstrasser DF; Tosi P
Department of Molecular Biology, University of Siena, Italy.
Electrophoresis (GERMANY) Dec 1997, 18 (15) p2832-41, ISSN 0173-0835 Journal Code: ELE
Languages: ENGLISH
Document type: Clinical Trial; Journal Article; Randomized Controlled Trial
Record type: Completed
Reference two-dimensional (2-D) gels are presented for human breast ductal carcinoma and histologically normal tissue. Whole biopsy fragments were analyzed, including epithelial and nonepithelial components. Thirty-five spots have been assigned by gel matching to the human liver SWISS-2DPAGE reference map and/or to the human primary keratinocyte IPG map from the Danish Center for Human Genome. N-terminal microsequencing was applied to confirm randomly chosen matching assignments and to identify six new spots. Protein expression profiles in ductal carcinoma and in normal breast tissue appeared to be similar, except for a pattern consisting of 32 spots, which were highly expressed in all carcinoma specimens, and less intense and occasionally undetectable in normal tissue. This difference was statistically significant. Assignment has been obtained for several spots, namely GRP94, GRP78, GRP75, mitochondrial HSP60, calreticulin , protein disulfide isomerase, peptidyl-prolyl cis-trans isomerase, collagen-binding protein 2, fructose bisphosphate aldolase, glyceraldehyde-3-phosphate dehydrogenase, thioredoxin, cytochrome c oxidase VA subunit, tubulin beta isoform and macrophage migration inhibitory factor (MIF). The cancer - and tissue-specificity of the described pattern was assessed by matching to the Swiss-2DPAGE human liver, hepatoma, lymphoma, erythroleukemia reference maps. The pattern of 32 spots was found to be indicative of epithelial neoplasia.

2/AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09652247 98094361 PMID: 9430631
Cell wall 1,6-beta-glucan synthesis in Saccharomyces cerevisiae depends on ER glucosidases I and II, and the molecular chaperone BiP/Kar2p.
Simons JF; Ebersold M; Helenius A
Department of Cell Biology, Yale University School of Medicine, New

Haven, CT 06520-8002, USA.
EMBO journal (ENGLAND) Jan 15 1998, 17 (2) p396-405, ISSN 0261-4189
Journal Code: EMB
Contract/Grant No.: CA46128, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The role of glucose trimming in the endoplasmic reticulum of Saccharomyces cerevisiae was investigated using glucosidase inhibitors and mutant strains devoid of glucosidases I and II. These glucosidases are responsible for removing glucose residues from the N-linked core oligosaccharides attached to newly synthesized polypeptide chains. In mammalian cells they participate together with calnexin, calreticulin and UDP-glucose:glycoprotein glucosyltransferase in the folding and quality control of newly synthesized glycoproteins. In S.cerevisiae, glucosidase II is encoded by the GLS2 gene, and glucosidase I, as suggested here, by the CWH41 gene. Using castanospermine (an alpha-glucosidase inhibitor) and yeast strains defective in glucosidase I, glucosidase II and BiP/Kar2p, it was demonstrated that cell wall synthesis depends on the two glucosidases and BiP/Kar2p. In double mutants with defects in both BiP/Kar2p and either of the glucosidases the phenotype was particularly clear: synthesis of 1,6-beta-glucan a cell wall component was reduced; the cell wall displayed abnormal morphology; the cells aggregated; and their growth was severely inhibited . No defects in protein folding or secretion could be detected. We concluded that glucose trimming in S.cerevisiae is necessary for proper cell wall synthesis, and that the glucosidases function synergistically with BiP/Kar2p in this process.

2/AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09346940 97322351 PMID: 9177196
Aberrant retention of tyrosinase in the endoplasmic reticulum mediates accelerated degradation of the enzyme and contributes to the dedifferentiated phenotype of amelanotic melanoma cells.
Halaban R; Cheng E; Zhang Y; Moellmann G; Hanlon D; Michalak M; Setaluri V; Hebert DN
Department of Dermatology, Yale University School of Medicine, New Haven, CT 06520, USA. ruth.halaban@yale.edu
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Jun 10 1997, 94 (12) p6210-5, ISSN 0027-8424
Journal Code: PV3
Contract/Grant No.: AR39848, AR, NIAMS; AR41942, AR, NIAMS; CA44542, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The loss of tyrosinase, the key enzyme in melanin synthesis, has been implicated in the dedifferentiation of malignant melanocytes. The presence of tyrosinase transcripts and antigenic peptides in melanoma tumors prompted us to investigate whether the basis for the loss of the enzyme was proteolytic degradation. Toward this aim, we followed the kinetics of synthesis, degradation, processing, chaperone binding, inhibitor sensitivity, and subcellular localization of tyrosinase in normal and malignant melanocytes. We found that, in amelanotic melanoma cell lines, tyrosinase failed to reach the melanosome, the organelle for melanin synthesis, because it was retained in the endoplasmic reticulum (ER) and then degraded. Tyrosinase appeared mostly as a 70-kDa core-glycosylated, endoglycosidase H-sensitive, immature form bound to the ER chaperone calnexin and had a life-span of only 25% of normal. Maturation and transit

from the ER to the Golgi compartment was facilitated by lowering the temperature of incubation to 31 degrees C. Several proteasome inhibitors caused the accumulation of an approximately 60-kDa tyrosinase doublet that was more prominent in malignant than in normal melanocytes and promoted, to various degrees, the maturation of tyrosinase in melanoma cells and the translocation of the enzyme to melanosomes. The appearance of ubiquitinated tyrosinase after treatment of normal melanocytes with N-acetyl-L-leucinyl-L-leucinal-L-norleucinal reinforced our notion that some tyrosinase is normally degraded by proteasomes. Proteolysis of tyrosinase by proteasomes is consistent with the production of antigenic tyrosinase peptides that are presented to the immune system by major histocompatibility complex class I molecules.

2/AB/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08849652 96211761 PMID: 8630223
Control of tumor progression by maintenance of apoptosis.
Bruchovsky N; Snoek R; Rennie PS; Akakura K; Goldenberg LS; Gleave M
Department of Cancer Endocrinology, BC Cancer Agency, Vancouver, British Columbia, Canada.
Prostate. Supplement (UNITED STATES) 1996, 6 p13-21, ISSN 1050-5881 Journal Code: ANH
Languages: ENGLISH
Document type: Journal Article; Review; Review, Tutorial
Record type: Completed
The ability to induce multiple apoptotic regressions of an androgen-dependent tumor cell population by repeated cycles of androgen withdrawal and replacement may be advantageous in therapeutic strategies aimed at delaying or preventing tumor progression. With greater insight into factors that either initiate or limit apoptosis, more efficient application of intermittent therapy might be achieved, especially if methods could be devised to increase the length or number of treatment cycles. Both calreticulin and clusterin represent proteins with a potential role in the regulation of apoptosis. Calreticulin may inhibit target gene transcription by interacting with steroid hormone receptors, thereby masking their DNA-binding sites and triggering the onset of the apoptotic process. Clusterin, on the other hand, is a membrane-stabilizing protein that appears to be involved in limiting the autophagic lysis of epithelial cells during apoptosis. Also, the increasing tendency for nuclear localization of clusterin after androgen withdrawal may preserve the nuclear environment, limiting the lethal effect of treatment . Thus, tumor progression, characterized by the loss of apoptotic potential, appears to be linked in part to the inappropriate activation of TRPM-2 gene, which accounts for the constitutive expression of clusterin.

2/AB/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08776871 95403383 PMID: 7673176
Components of the protein synthesis and folding machinery are induced in vascular smooth muscle cells by hypertrophic and hyperplastic agents. Identification by comparative protein phenotyping and microsequencing.
Patton WF; Erdjument-Bromage H; Marks AR; Tempst P; Taubman MB
Molecular Biology Program, Memorial Sloan-Kettering Cancer Center, New York, New York 10021, USA.
Journal of biological chemistry (UNITED STATES) Sep 8 1995, 270 (36) p21404-10, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: 5 P30 CA08748-29, CA, NCI; RO1 HL43302, HL, NHLBI;

RO1 NS29814, NS, NINDS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Vascular smooth muscle cells (VSMC) are the principal cellular component of the blood vessel wall. Atherosclerosis, hypertension, and angiogenesis are associated with abnormal VSMC growth. Angiotensin II is hypertrophic for cultured adult rat aortic VSMC, whereas platelet-derived growth factor and serum are hyperplastic. To identify changes in specific proteins associated with either hyperplastic or hypertrophic growth, high resolution two-dimensional gel electrophoresis was performed on extracts from quiescent rat aortic VSMC and from VSMC exposed for 24 h to growth factors (10% fetal calf serum, platelet-derived growth factor, or angiotensin II). 12 proteins were up-regulated and 5 down-regulated by treatment with growth factors. Eight of the up-regulated and one of the down-regulated proteins were identified by internal protein microsequencing from electroblotted two-dimensional gels or by co-electrophoresis of purified proteins in two-dimensional gels. Four of the proteins up-regulated by growth factors were identified as mediators of protein folding. These were heat shock proteins, HSP-60 and HSP-70, protein disulfide isomerase, and protein disulfide isomerase isozyme Q-2. Additional proteins were identified as elongation factor EF-1 beta, a component of the protein synthesis apparatus, and calreticulin , another putative molecular chaperone. Vimentin and actin were also up-regulated, whereas an isoform of myosin heavy chain was down-regulated. Hyperplastic and hypertrophic growth were accompanied by similar changes in protein expression, suggesting that both types of growth require up-regulation of the protein synthesis and folding machinery.

2/AB/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08491838 95229636 PMID: 7713923

Calreticulin , an antithrombotic agent which binds to vitamin K-dependent coagulation factors, stimulates endothelial nitric oxide production, and limits thrombosis in canine coronary arteries.

Kuwabara K; Pinsky DJ; Schmidt AM; Benedict C; Brett J; Ogawa S; Broekman MJ; Marcus AJ; Sciacca RR; Michalak M; et al
Department of Physiology, Columbia University, College of Physicians and Surgeons, New York, New York 10032, USA.

Journal of biological chemistry (UNITED STATES) Apr 7 1995, 270 (14) p8179-87, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: AG00602, AG, NIA; HL34625, HL, NHLBI; HL42833, HL, NHLBI; +
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Coagulation Factor IX/IXa has been shown to bind to cellular surfaces, and Factor IXa expresses its procoagulant activity by assembling into the intrinsic Factor X activating complex (Factors IXa/VIIIa/X), which also forms on membrane surfaces. This led us to identify cellular proteins which bind Factor IX/IXa; an approximately 55-kDa polypeptide was purified to homogeneity from bovine lung extracts based on its capacity to bind 125I-Factor IX in a dose-dependent and saturable manner. From protein sequence data of the amino terminus and internal peptides, the approximately 55-kDa polypeptide was identified as calreticulin , a previously identified intracellular calcium-binding protein. Recombinant calreticulin bound vitamin K-dependent coagulation factors, 125I-Factor IX, 125I-Factor X, and 125I-prothrombin (Kd values of approximately 2.7, 3.2, and 8.3 nM, respectively), via interaction with its C-domain, although

it did not affect the coagulant properties of these proteins. 125I-Calreticulin also bound to endothelial cells in vitro (Kd approximately 7.4 nM), and mouse infusion studies showed an initial rapid phase of clearance in which calreticulin could be localized on the vascular endothelium. Exposure of endothelial cells to calreticulin led to dose-dependent, immediate, and sustained increase in the production of nitric oxide, as measured using a porphyrinic microsensor. In a canine electrically induced thrombosis model, intracoronary infusion of calreticulin (n = 7) prevented occlusion of the left circumflex coronary artery in a dose-dependent manner compared with vehicle-treated controls (n = 5). These results indicate that calreticulin interacts with the endothelium to stimulate release of nitric oxide and inhibit clot formation.

2/AB/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08279261 95050664 PMID: 7961812
Decreasing calreticulin expression lowers the Ca2+ response to bradykinin and increases sensitivity to ionomycin in NG-108-15 cells.
Liu N; Fine RE; Simons E; Johnson RJ
Department of Biochemistry, Boston University School of Medicine, Massachusetts 02118.
Journal of biological chemistry (UNITED STATES) Nov 18 1994, 269 (46) p28635-9, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: AG-00115, AG, NIA; R37 AG-05894, AG, NIA
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
It has been suggested that the multifunctional protein, calreticulin , is a major calcium sequestering protein in the inositol 1,4,5-trisphosphate receptor-containing endoplasmic reticulum subcompartment. In neuroblastoma X glioma NG-108-15 cells, bradykinin can effectively stimulate the release of inositol 1,4,5-trisphosphate and cause a cytosolic calcium transient. To explore the function of calreticulin as an intracellular calcium sequestering protein, we investigated calcium dynamics in NG-108-15 cells after treatment with an antisense oligonucleotide against calreticulin , CrtAS1. Cells treated with either CrtAS1 or the corresponding sense oligonucleotide CrtPS1 were examined for their calreticulin content by Western blotting, the amplitude of their calcium transient in response to bradykinin, and their sensitivity toward the calcium ionophore, ionomycin. Treatment with CrtAS1 decreased the amount of calreticulin in comparison to CrtPS1-treated and untreated control cells. At the same time, CrtAS1-treated cells had a significantly reduced calcium response to bradykinin and were more sensitive to ionomycin-induced cell death. These data show that the level of calreticulin expression is directly related to the calcium storage capacity of the inositol 1,4,5-trisphosphate-sensitive calcium pool and indicate a direct relationship between the level of calreticulin and the protection against cytotoxic calcium overload.

2/AB/14 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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12861139 BIOSIS NO.: 200100068288
Aluminum-induced 1fwdarw3-beta-D-glucan inhibits cell-to-cell trafficking of molecules through plasmodesmata. A new mechanism of aluminum toxicity in plants.

AUTHOR: Sivaguru Mayandi; Fujiwara Toru; Samaj Josef; Baluska Frantisek; Yang Zhenming; Osawa Hiroki; Maeda Takanori; Mori Tomoko; Volkmann Dieter ; Matsumoto Hideaki(a)
AUTHOR ADDRESS: (a)Research Institute for Bioresources, Okayama University, Kurashiki, 710-0046: hmatsumo@rib.okayama-u.ac.jp**Japan
JOURNAL: Plant Physiology (Rockville) 124 (3):p991-1005 November, 2000
MEDIUM: print
ISSN: 0032-0889
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Symplastic intercellular transport in plants is achieved by plasmodesmata (PD). These cytoplasmic channels are well known to interconnect plant cells to facilitate intercellular movement of water, nutrients, and signaling molecules including hormones. However, it is not known whether Al may affect this cell-to-cell transport process, which is a critical feature for roots as organs of nutrient/water uptake. We have microinjected the dye lucifer yellow carbohydrazide into peripheral root cells of an Al-sensitive wheat (Triticum aestivum cv Scout 66) either before or after Al treatment and followed the cell-to-cell dye-coupling through PD. Here we show that the Al-induced root growth inhibition is closely associated with the Al-induced blockage of cell-to-cell dye coupling. Immunofluorescence combined with immuno-electron microscopic techniques using monoclonal antibodies against 1fwdarw3-beta-D-glucan (callose) revealed circumstantial evidence that Al-induced callose deposition at PD may responsible for this blockage of symplastic transport. Use of 2-deoxy-D-glucose, a callose synthesis inhibitor, allowed us to demonstrate that a reduction in callose particles correlated well with the improved dye-coupling and reduced root growth inhibition . While assessing the tissue specificity of this Al effect, comparable responses were obtained from the dye-coupling pattern in tobacco (Nicotiana tabacum) mesophyll cells. Analyses of the Al-induced expression of PD-associated proteins, such as calreticulin and unconventional myosin VIII, showed enhanced fluorescence and co-localizations with callose deposits. These results suggest that Al-signal mediated localized alterations to calcium homeostasis may drive callose formation and PD closure. Our data demonstrate that extracellular Al-induced callose deposition at PD could effectively block symplastic transport and communication in higher plants.

2000

2/AB/15 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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10912113 BIOSIS NO.: 199799533258
Calreticulin expression inhibits prostate cancer cell death.
AUTHOR: Zhu N; Pewitt E B; Wang Z
AUTHOR ADDRESS: Northwestern Univ., Chicago, IL 60611**USA
JOURNAL: Proceedings of the American Association for Cancer Research Annual Meeting 38 (0):p575 1997
CONFERENCE/MEETING: Eighty-eighth Annual Meeting of the American Association for Cancer Research San Diego, California, USA April 12-16, 1997
ISSN: 0197-016X
RECORD TYPE: Citation
LANGUAGE: English

1997

2/AB/16 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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10433535 BIOSIS NO.: 199699054680
Genomic mechanisms involved in the pleiotropic actions of 1,25-dihydroxyvitamin D-3.
AUTHOR: Christakos Sylvia(a); Raval-Pandya Mihali; Wernyj Roman P; Yang Wen
AUTHOR ADDRESS: (a)Dep. Biochem. Mol. Biol., Univ. Med. Dentistry New Jersey, New Jersey Med. Sch., 185 South Orang**USA
JOURNAL: Biochemical Journal 316 (2):p361-371 1996
ISSN: 0264-6021
DOCUMENT TYPE: Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The biologically active metabolite of vitamin D (cholecalciferol), i.e. 1,25-dihydroxyvitamin D-3 (1,25(OH)-2D-3), is a secosteroid hormone whose mode of action involves stereospecific interaction with an intracellular receptor protein (vitamin D receptor; VDR). 1,25(OH)-2D-3 is known to be a principal regulator of calcium homeostasis, and it has numerous other physiological functions including inhibition of proliferation of cancer cells, effects on hormone secretion and suppression of T-cell proliferation and cytokine production. Although the exact mechanisms involved in mediating many of the different effects of 1,25(OH)-2D-3 are not completely defined, genomic actions involving the VDR are clearly of major importance. Similar to other steroid receptors, the VDR is phosphorylated; however, the exact functional role of the phosphorylation of the VDR remains to be determined. The VDR has been reported to be regulated by 1,25(OH)-2D-3 and also by activation of protein kinases A and C, suggesting co-operativity between signal transduction pathways and 1,25(OH)-2D-3 action. The VDR binds to vitamin D-responsive elements (VDREs) in the 5'flanking region of target genes. It has been suggested that VDR homodimerization can occur upon binding to certain VDREs but that the VDR/retinoid X receptor (RXR) heterodimer is the functional transactivating species. Other factors reported to be involved in VDR-mediated transcription include chicken ovalbumin upstream promoter (COUP) transcription factor, which is involved in active silencing of transcription, and transcription factor IIB, which has been suggested to play a major role following VDR/RXR heterodimerization. Newly identified vitamin D-dependent target genes include those for Ca-2+/Mg-2+-ATPase in the intestine and p21 in the myelomonocytic U937 cell line. Elucidation of the mechanisms involved in the multiple actions of 1,25(OH)-2D-3 will be an active area of future research.

1996

2/AB/17 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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09047410 BIOSIS NO.: 199497055780
Antisense to calreticulin inhibits endothelial cell proliferation.
AUTHOR: Kaplan Barry M; Hatcher Victor; Kaplan Matthew; Welikson Robert; Buttrick Peter M
AUTHOR ADDRESS: Montefiore Med. Cent., Albert Einstein Coll. Med., Bronx,

NY**USA
JOURNAL: Circulation 88 (4 PART 2):pI190 1993
CONFERENCE/MEETING: 66th Scientific Sessions of the American Heart Association Atlanta, Georgia, USA November 8-11, 1993
ISSN: 0009-7322
RECORD TYPE: Citation
LANGUAGE: English
1993

2/AB/18 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2001 Inst for Sci Info. All rts. reserv.

07147393 Genuine Article#: 129ED Number of References: 33
Title: Protection of mammalian cells from the toxicity of bleomycin by expression of a bleomycin-binding protein gene from Streptomyces verticillus (ABSTRACT AVAILABLE)
Author(s): Kumagai T; Sugiyama M (REPRINT)
Corporate Source: HIROSHIMA UNIV,SCH MED, INST PHARMACEUT SCI, MINAMI KU, KASUMI 1-2-3/HIROSHIMA 7348551//JAPAN/ (REPRINT); HIROSHIMA UNIV,SCH MED, INST PHARMACEUT SCI, MINAMI KU/HIROSHIMA 7348551//JAPAN/
Journal: JOURNAL OF BIOCHEMISTRY, 1998, V124, N4 (OCT), P835-841
ISSN: 0021-924X Publication date: 19981000
Publisher: JAPANESE BIOCHEMICAL SOC, ISHIKAWA BLDG-3F, 25-16 HONGO-5-CHOME, BUNKYO-KU, TOKYO 113, JAPAN
Language: English Document Type: ARTICLE
Abstract: A gene, blmA, encodes a bleomycin (Bm)-binding protein, designated BLMA, from Bm-producing Streptomyces verticillus and confers resistance to Pm in Streptomyces and Escherichia coli cells, In the present study, by transfection of the gene into COS-1 cells with a plasmid designated pEF-BOS/blmA, which contains a strong promoter from the human polypeptide chain elongation factor la, we transiently overproduced BLMA at a high level of approximately 4% of the whole cell protein, Although NIH/3T3 cells transfected with pEF-BOS/blmA, designated NIH/3T3-BR cells, stably expressed BLMA, its expression level was about 0.1% of the total protein. Using an anti-BLMA monoclonal antibody reported previously [Sugiyama et al, (1995) FEES Lett. 362, 80-84], we revealed that BLMA is localized in the nucleus of pEF-BOS/blmA-transfected COS-1 and NIH/3T3-BR cells, Semi-permeabilized nuclear transport experiments showed that BLMA penetrates the nuclear envelope by energy- and transporter-independent passive diffusion, suggesting that the karyophilic nature of BLMA may be due to the acidic nature of the protein. NIH/ 3T3-BR cells were 130-fold more resistant to Bm than the host cells, NIH/3T3 cells exhibited a swollen nuclear envelope and a malformed spindle body and overexpressed at least 4 kinds of stress proteins including calreticulin and mitochondrial matrix protein P1 when exposed to 25 mu g/ml of Bm, whereas NIH/3T3-BR cells grew without morphological alteration and expressed no stress proteins under the same conditions. Furthermore, reverse transcription-polymerase chain reaction and Northern blot analysis showed that the expression of interleukin-6, an inflammatory cytokine, is activated by addition of Bm in NIH/3T3 cells, but not in the NIH/3T3-BR cells. These results suggest that BLMA contributes to protection of mammalian cells from the inflammatory effect of Bm.

2/AB/19 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2001 Inst for Sci Info. All rts. reserv.

06198007 Genuine Article#: YA930 Number of References: 49
Title: Phenotypic knockout of HIV type 1 chemokine coreceptor CCR-5 by intrakines as potential therapeutic approach for HIV-1 infection (ABSTRACT AVAILABLE)
Author(s): Yang AG; Bai XF; Huang XF; Yao CP; Chen SY (REPRINT)
Corporate Source: WAKE FOREST UNIV,BOWMAN GRAY SCH MED, CTR COMPREHENS CANC, DEPT CANC BIOL, 300 S HAWTHORNE R/WINSTON SALEM//NC/27157 (REPRINT); WAKE FOREST UNIV,BOWMAN GRAY SCH MED, CTR COMPREHENS CANC, DEPT CANC BIOL/WINSTON SALEM//NC/27157; WAKE FOREST UNIV,BOWMAN GRAY SCH MED, CTR COMPREHENS CANC, DEPT COMPARAT MED/WINSTON SALEM//NC/27157
Journal: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, 1997, V94, N21 (OCT 14), P11567-11572
ISSN: 0027-8424 Publication date: 19971014
Publisher: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW, WASHINGTON, DC 20418
Language: English Document Type: ARTICLE
Abstract: A genetic defect in a CC-chemokine receptor (CCR)-5, the principal coreceptor for the macrophage-tropic HIV type 1 (HIV-1), recently was found to naturally protect CCR-5-defective, but healthy, individuals from HIV-1 infection, In this study, we mimic the natural resistance of the CCR-5-defective individuals by designing a strategy to phenotypically knock out CCR-5. The inactivation of the CCR-5 coreceptor is accomplished by targeting a modified CC chemokine to the endoplasmic reticulum to block the surface expression of newly synthesized CCR-5, The lymphocytes transduced to express the intracellular chemokine, termed ''intrakine,'' were found to be viable and resistant to macrophage-tropic HIV-1 infection, Thus, this gene-based intrakine strategy targeted at the conserved cellular receptor for the prevention of HIV-1 entry should have significant advantages over currently described approaches for HIV-1 therapy.

2/AB/20 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2001 Inst for Sci Info. All rts. reserv.

06037339 Genuine Article#: XQ799 Number of References: 33
Title: The critical N-linked glycan of murine leukemia virus envelope protein promotes both folding of the C-terminal domains of the precursor polyprotein and stability of the postcleavage envelope complex (ABSTRACT AVAILABLE)
Author(s): Li ZY; Pinter A; Kayman SC (REPRINT)
Corporate Source: PUBL HLTH RES INST,LAB RETROVIRAL BIOL, 455 1ST AVE/NEW YORK//NY/10016 (REPRINT); PUBL HLTH RES INST,LAB RETROVIRAL BIOL/NEW YORK//NY/10016; NYU,SCH MED, DEPT MICROBIOL/NEW YORK//NY/10016
Journal: JOURNAL OF VIROLOGY, 1997, V71, N9 (SEP), P7012-7019
ISSN: 0022-538X Publication date: 19970900
Publisher: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171
Language: English Document Type: ARTICLE
Abstract: The infectivity of Friend ecotropic murine leukemia virus was previously shown to be highly sensitive to modification in its envelope protein (Env) at only one of the eight signals for N-linked glycan attachment, the fourth from the N terminus (gs4). In the present study, a set of six single-amino-acid substitutions in or near gs4 was used to determine the function of this region of Env and the role played by the glycan itself, One mutant that lacked the gs4 glycan was fully infectious, while one that retained this glycan was completely noninfectious, indicating that the gs4 glycan per se is not required for Env function, Infectivity correlated with the level of mature Env complex incorporated into virus particles, which was determined by the

severity of defects in transport of the envelope precursor protein (gPrEnv) from the endoplasmic reticulum into the Golgi apparatus, in cleavage of gPrEnv into the two envelope subunits (the surface protein [SU] and the transmembrane protein [TM]), and in the association of SU with cellular membranes, All of the mutants induced the wild-type level of superinfection interference, indicating that the gs4 region mutations did not interfere with proper folding of the N-terminal domain of SU, These results suggest that the gs4 region mediates folding of the C-terminal domains of gPrEnv and stability of the interaction between SU and TM. Although the gs4 glycan was not essential for infectivity, processing of all mutant Envs lacking this glycan was significantly impaired, suggesting that efficient folding of gPrEnv requires a glycan at this position, The conservation of a glycosylation site homologous to gs4 across a broad range of retroviruses suggests that this sequence may play a similar role in many retroviral Envs.

2/AB/21 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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06022718 Genuine Article#: XP983 Number of References: 34
Title: Biological role of tyrosinase related protein and its biosynthesis and transport from TGN to stage I melanosome, late endosome, through gene transfection study (ABSTRACT AVAILABLE)
Author(s): Jimbow K (REPRINT) ; Gomez PF; Toyofuku K; Chang D; Miura S; Tsujiya H; Park JS
Corporate Source: UNIV ALBERTA,DIV DERMATOL & CUTANEOUS SCI, HERITAGE MED RES CTR 260G, FAC MED/EDMONTON/AB T6G 2S2/CANADA/ (REPRINT); SAPPORO MED UNIV,SCH MED, DEPT DERMATOL, CHUO KU/SAPPORO/HOKKAIDO 060/JAPAN/
Journal: PIGMENT CELL RESEARCH, 1997, V10, N4 (AUG), P206-213
ISSN: 0893-5785 Publication date: 19970800
Publisher: MUNKSGAARD INT PUBL LTD, 35 NORRE SOGADE, PO BOX 2148, DK-1016 COPENHAGEN, DENMARK
Language: English Document Type: REVIEW
Abstract: Tyrosinase-related protein (TRP)-1 is one of the most abundant melanosomal glycoproteins involved in melanogenesis. This report summarizes our recent research efforts related to the biological role and biosynthesis of TRP-1 and its transport from TGN (trans-Golgi network) to the stage I melanosome. Our UV irradiation and tyrosinase and TRP-1 cDNA co-transfection studies indicated that human TRP-1 is involved in nob only melanogenesis but also prevention of melanocyte death, which may occur during biosynthesis of melanin pigment in the presence of tyrosinase. Furthermore, a coordinated gene interaction was indicated between tyrosinase and TRI)-1, resulting in upregulation of mRNA and protein expression of LAMP (lysosome-associated membrane protein)-1 that would directly prevent the tyrosinase-mediated programmed cell death of melanocytes, Similar to tyrosinase, however TRP-1 appears to require a molecular chaperone, calnexin, which we have cloned recently, Our cDNA transfection study of tyrosinase with calnexin showed clearly the necessity of calnexin in order to have efficient, functional activity of melanosomal glycoprotein, especially tyrosinase. Once glycosylation is completed, TRP-1 will be transported from TGN to the stage I melanosome, At this stage, TRP-1 will have its own target signal, in particular tyrosine-rich leucine residues in cytoplasmic tail. Our TRP-1 cDNA transfection and immunoelectron microscopy study shows that TRP-1 will be transported through small vesicles, probably non clathrin-coated type, to large vacuoles, identical to the MPR (mannose-6-phosphate receptor)-positive, late endosomes. In this transport process, a low

molecular weight G-protein, rab-7, was isolated from the purified melanosomal protein on 2D-PAGE and identified by subsequent sequencing and PCR amplification. Confocal microscopy with double immunostaining and immunoelectron microscopy confirmed the co-localization of rab-7 and TRP-1 in the melanosomes with early stages of maturation (I-III). Furthermore, this process will also be regulated by phosphatidylinositol 3-kinase (PI-3 kinase).

2/AB/22 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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05929708 Genuine Article#: XH428 Number of References: 49
Title: Calreticulin biosynthesis and processing in human myeloid cells: Demonstration of signal peptide cleavage and N-glycosylation (ABSTRACT AVAILABLE)
Author(s): Denning GM; Leidal KG; Holst VA; Iyer SS; Pearson DW; Clark JR; Nauseef WM; Clark RA (REPRINT)
Corporate Source: UNIV TEXAS,HLTH SCI CTR, DEPT MED, 7703 FLOYD CURL DR/SAN ANTONIO//TX/78284 (REPRINT); UNIV TEXAS,HLTH SCI CTR, DEPT MED/SAN ANTONIO//TX/78284; DEPT VET AFFAIRS MED CTR,DEPT MED/IOWA CITY//IA/52242; UNIV IOWA,/IOWA CITY//IA/; S TEXAS VET HLTH CARE SYST,AUDIE L MURPHY DIV, DEPT MED/SAN ANTONIO//TX/
Journal: BLOOD, 1997, V90, N1 (JUL 1), P372-381
ISSN: 0006-4971 Publication date: 19970701
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399
Language: English Document Type: ARTICLE
Abstract: Calreticulin is a soluble endoplasmic reticulum protein comprising the major storage reservoir for inositol trisphosphate-releasable calcium. Although its highly conserved primary structure and a wide range of functions have been well described, less attention has been paid to its biosynthesis, particularly in human tissues. We report analyses of synthesis, proteolytic processing and glycosylation of human calreticulin , In both HL-60 and PLB-985 myeloid cell lines calreticulin was immunoprecipitated as a single 60-kD species without evidence of precursor forms. However, in vitro cell-free synthesis produced a 62-kD primary translation product, which in the presence of microsomal membranes, was processed by cotranslational signal peptide cleavage to a 60-kD species that comigrated with mature calreticulin produced in myeloid cells, Neither tunicamycin treatment of the cells nor endoglycosidase digestion of calreticulin resulted in any forms other than the 60-kD protein on sodium dodecyl sulfate-polyacrylamide gel electrophoresis analysis, suggesting that the potential site for N-glycosylation at asparagine-327 was unmodified, However, oxidative derivatization of carbohydrate components with digoxigenin showed that human calreticulin produced in either HL-60 cells or Sf9 insect cells is glycosylated, indicating that glycosylated and nonglycosylated human calreticulin have indistinguishable electrophoretic mobilities, Direct measurement by phenol-H2SO4 confirmed the presence of carbohydrate on recombinant human calreticulin , These data show that human myeloid calreticulin undergoes cotranslational signal peptide cleavage and posttranslational N-linked glycosylation, Although glycosylation of calreticulin has been shown in rat liver and bovine liver and brain, it has been reported to be lacking in other tissues including human lymphocytes. (C) 1997 by The American Society of Hematology.

2/AB/23 (Item 6 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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05900170 Genuine Article#: XF329 Number of References: 32
Title: Inhibition of N-glycan processing in B16 melanoma cells results in inactivation of tyrosinase but does not prevent its transport to the melanosome (ABSTRACT AVAILABLE)
Author(s): Petrescu SM; Petrescu AJ; Titu HN; Dwek RA; Platt FM (REPRINT)
Corporate Source: UNIV OXFORD,GLYCOBIOL INST, S PARKS RD/OXFORD OX1 3QU//ENGLAND/ (REPRINT); UNIV OXFORD,GLYCOBIOL INST/OXFORD OX1 3QU//ENGLAND/; INST BIOCHEM,/BUCHAREST 77700 17//ROMANIA/
Journal: JOURNAL OF BIOLOGICAL CHEMISTRY, 1997, V272, N25 (JUN 20), P 15796-15803
ISSN: 0021-9258 Publication date: 19970620
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814
Language: English Document Type: ARTICLE
Abstract: Tyrosinase is the key enzyme in melanin biosynthesis, catalyzing multiple steps ill this pathway, The mature glycoprotein is transported from the Golgi to the melanosome where melanin biosynthesis occurs, In this study, we have investigated the effects of inhibitors of N-glycan processing on the synthesis, transport, and catalytic activity of tyrosinase. When B16 mouse melanoma cells were cultured ill the presence of N-butyldeoxynojirimycin , an inhibitor of the endoplasmic reticulum-processing enzymes alpha-glucosidases I and II, the enzyme was synthesized and transported to the melanosome but almost completely lacked catalytic activity, The cells contained only 2% of the melanin found in untreated cells, Structural analysis of the N-glycans from N-butyldeoxgngirimycin-treated B16 cells demonstrated that three oligosaccharide structures (Glc(3)Man(7-9)) predominated, Removal of the glucose residues with alpha-glucosidases I and II failed to restore enzymatic activity, suggesting that the glucosylated N-glycans do not sterically interfere with the enzyme's active sites, The mannosidase inhibitor deoxymannojirimycin had no effect. on catalytic activity suggesting that the retention of glucosylated N-glycans results in the inactivation of this enzyme, The retention of glucosylated N-glycans does not therefore result in misfolding and degradation of the glycoprotein, as the enzyme is transported to the melanosome, but may cause conformational changes in its catalytic domains.

2/AB/24 (Item 7 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2001 Inst for Sci Info. All rts. reserv.

05647712 Genuine Article#: WN392 Number of References: 293
Title: Intracellular protein transport to the thyrocyte plasma membrane: Potential implications for thyroid physiology (ABSTRACT AVAILABLE)
Author(s): Arvan P (REPRINT) ; Kim PS; Kuliawat R; Prabakaran D; Muresan Z; Yoo SE; AbuHossain S
Corporate Source: YESHIVA UNIV ALBERT EINSTEIN COLL MED,DIV ENDOCRINOL/BRONX//NY/10461 (REPRINT); BETH ISRAEL DEACONESS MED CTR,DEPT MED, DIV ENDOCRINOL/BOSTON//MA/02215
Journal: THYROID, 1997, V7, N1 (FEB), P89-105
ISSN: 1050-7256 Publication date: 19970200
Publisher: MARY ANN LIEBERT INC PUBL, 2 MADISON AVENUE, LARCHMONT, NY 10538
Language: English Document Type: REVIEW
Abstract: We present a snapshot of developments in epithelial biology that may prove helpful in understanding cellular aspects of the machinery designed for the synthesis of thyroid hormones on the thyroglobulin precursor. The functional unit of the thyroid gland is the follicle,

delimited by a monolayer of thyrocytes. Like the cells of most simple epithelia, thyrocytes exhibit specialization of the cell surface that confronts two different extracellular environments-apical and basolateral, which are separated by tight junctions. Specifically, the basolateral domain faces the interstitium/bloodstream, while the apical domain is in contact with the lumen that is the primary target for newly synthesized thyroglobulin secretion and also serves as a storage depot for previously secreted protein. Thyrocytes use their polarity in several important ways, such as for maintaining basolaterally located iodide uptake and T-4 deiodination, as well apically located iodide efflux and iodination machinery. The mechanisms by which this organization is established, fall in large part under the more general cell biological problem of intracellular sorting and trafficking of different proteins en route to the cell surface. Nearly all exportable proteins begin their biological life after synthesis in an intracellular compartment known as the endoplasmic reticulum (ER), upon which different degrees of difficulty may be encountered during nascent polypeptide folding and initial export to the Golgi complex. In these initial stages, ER molecular chaperones can assist in monitoring protein folding and export while themselves remaining as resident proteins of the thyroid ER. After export from the ER, most subsequent sorting for protein delivery to apical or basolateral surfaces of thyrocytes occurs within another specialized intracellular compartment known as the trans-Golgi network. Targeting information encoded in secretory proteins and plasma membrane proteins can be exposed or buried at different stages along the export pathway, which is likely to account for sorting and specific delivery of different newly-synthesized proteins. Defects in either burying or exposing these structural signals, and consequent abnormalities in protein transport, may contribute to different thyroid pathologies.

2/AB/25 (Item 8 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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03957124 Genuine Article#: QV348 Number of References: 29
Title: A SECRETED CALRETICULIN PROTEIN IN IXODID TICK (AMBLYOMMA-AMERICANUM) SALIVA (Abstract Available)
Author(s): JAWORSKI DC; SIMMEN FA; LAMOREAUX W; COONS LB; MULLER MT; NEEDHAM GR
Corporate Source: UNIV MARYLAND,SCH MED,DEPT MICROBIOL & IMMUNOL,655 W BALTIMORE ST/BALTIMORE//MD/21201; OHIO STATE UNIV,DEPT ENTOMOL,ACAROL LAB/COLUMBUS//OH/43210; UNIV FLORIDA,DEPT DAIRY & POULTRY SCI/GAINESVILLE//FL/32611; UNIV FLORIDA,ANIM & CELL BIOL PROGRAM/GAINESVILLE//FL/32611; MEMPHIS STATE UNIV,DEPT BIOL,CTR ELECTRON MICROSCOPY/MEMPHIS//TN/38152; OHIO STATE UNIV,DEPT MOLEC GENET/COLUMBUS//OH/43210
Journal: JOURNAL OF INSECT PHYSIOLOGY, 1995, V41, N4 (APR), P369-375
ISSN: 0022-1910
Language: ENGLISH Document Type: ARTICLE
Abstract: A complementary DNA clone from salivary glands of feeding female Amblyomma americanum ticks has been characterized as encoding calreticulin . Calreticulin , a major endoplasmic reticulum (ER) calcium-binding protein, appears to be secreted in Amblyomma and Dermacentor saliva. Evidence is accummulating that calreticulin performs roles unrelated to calcium storage, Unlike most known calreticulins, tick-secreted calreticulin lacks the ER retention signal, KDEL. This is the first molecular cloning of a specific tick salivary gland protein. The finding of a secreted calreticulin in tick saliva suggests a role for calreticulin in blood feeding through

host immunosuppression or antihemostasis.

2/AB/26 (Item 1 from file: 35)
DIALOG(R)File 35:Dissertation Abs Online
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01735010 AADAAI9960251
Identification and characterization ofp137 a differentially regulated cardiac marker of embryonic trichloroethylene exposure
Author: Collier, John Michael, II
Degree: Ph.D.
Year: 1999
Corporate Source/Institution: The University of Arizona (0009)
Source: VOLUME 61/02-B OF DISSERTATION ABSTRACTS INTERNATIONAL. PAGE 636. 119 PAGES

Embryonic trichloroethylene (TCE) exposure was previously shown to be associated with an increased incidence of cardiac birth defects. Although embryo data are lacking exposure studies on adult animals show an association between halogenated hydrocarbon exposure and modifications in gene expression. The present study was undertaken to identify embryonic mRNA transcripts differentially expressed following TCE or metabolite exposure. This study identified numerous differentially regulated transcripts following halogenated hydrocarbon exposure. Examples of upregulated transcripts include stress responsive genes (Hsp 70, Hsp 70 cognate), a Ca<super>2+</super>-ATPase, calreticulin and serum response factor while downregulated transcripts include Midkine (RARP), numerous ribosomal proteins (8s, 18s, 24s), p137 and vimentin. p137 was a candidate sequence marked for further study to determine whether this sequence could be utilized as a molecular marker of TCE exposure. p137 showed a correlation between increased levels of maternal TCE exposure and decreased levels of transcript expressed in E11 fetal tissue. Immunohistochemical staining using an affinity purified antibody to p137 demonstrates widespread expression in rat E11 and chicken St. 17 embryos. p137 protein is broadly expressed in chicken St. 13 through St. 22 heart, but by St. 29 becomes more restricted in the ventricular myocardium with continued endocardial expression. At stages between St. 13 and St. 17 in chick embryos the ectodermal epithelium, yolk sac epithelium, dermatome, developing optic vesicle and neural tube express p137 protein. To explore potential function of p137, atrioventricular explants were exposed to affinity purified p137 antibody. Results show that p137 antibody treatment blocks epithelial-mesenchymal transformation of endothelial cells <italic>in-vitro</italic>. This study shows that p137 is expressed during rat and chicken mid-gestation in heart and other epithelial tissue derivatives and appears to play a role in the epithelial-mesenchymal transformation of the cardiac atrioventricular cushions. p137 is identified as a useful marker of developmental exposure to halogenated hydrocarbons and its altered expression may contribute to the phenotype of the affected heart.

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DIALOG(R)File 71:ELSEVIER BIOBASE
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01604659 2000264530
Aluminum-induced 1<rt arrow>3-beta-D-glucan inhibits cell-to-cell trafficking of molecules through plasmodesmata. A new mechanism of aluminum toxicity in plants
Sivaguru M.; Fujiwara T.; Samaj J.; Baluska F.; Yang Z.; Osawa H.; Maeda T.

; Mori T.; Volkmann D.; Matsumoto H.
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Journal: Plant Physiology, 124/3 (991-1005), 2000, United States
CODEN: PLPHA
ISSN: 0032-0889
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 75

Symplastic intercellular transport in plants is achieved by plasmodesmata (PD). These cytoplasmic channels are well known to interconnect plant cells to facilitate intercellular movement of water, nutrients, and signaling molecules including hormones. However, it is not known whether Al may affect this cell-to-cell transport process, which is a critical feature for roots as organs of nutrient/water uptake. We have microinjected the dye lucifer yellow carbohydrazide into peripheral root cells of an Al-sensitive wheat (Triticum aestivum cv Scout 66) either before or after Al treatment and followed the cell-to-cell dye-coupling through PD. Here we show that the Al-induced root growth inhibition is closely associated with the Al-induced blockage of cell-to-cell dye coupling. Immunofluorescence combined with immuno-electron microscopic techniques using monoclonal antibodies against 1<rt arrow>3-beta-D-glucan (callose) revealed circumstantial evidence that Al-induced callose deposition at PD may responsible for this blockage of symplastic transport. Use of 2-deoxy-D-glucose, a callose synthesis inhibitor, allowed us to demonstrate that a reduction in callose particles correlated well with the improved dye-coupling and reduced root growth inhibition . While assessing the tissue specificity of this Al effect, comparable responses were obtained from the dye-coupling pattern in tobacco (Nicotiana tabacum) mesophyll cells. Analyses of the Al-induced expression of PD-associated proteins, such as calreticulin and unconventional myosin VIII, showed enhanced fluorescence and co-localizations with callose deposits. These results suggest that Al-signal mediated localized alterations to calcium homeostasis may drive callose formation and PD closure. Our data demonstrate that extracellular Al-induced callose deposition at PD could effectively block symplastic transport and communication in higher plants.

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01490747 2000163425
Mesenchymal-epithelial transition in the developing metanephric kidney: Gene expression study by differential display
Plisov S.Y.; Ivanov S.V.; Yoshino K.; Dove L.F.; Plisova T.M.; Higinbotham K.G.; Karavanova I.; Lerman M.; Perantoni A.O.
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Journal: Genesis, 27/1 (22-31), 2000, United States
CODEN: GNESF
ISSN: 1526-954X
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 44

The developing metanephric kidney is a convenient model to study molecular events associated with epithelial cell differentiation. To determine the

genes involved in the defining event of this process, namely, the conversion of metanephric mesenchyme to the epithelium of the nephron, we applied differential display (DD) techniques. Explants of rat metanephric mesenchymes were induced to condense ex vivo with fibroblast growth factor 2 (FGF2) or to form tubules with FGF2 and conditioned medium (CM) from a cell line (RUB1) of ureteric bud, the renal inductive tissue. Three time points (6, 24, and 72 h) were chosen to track the dynamics of gene expression during morphogenesis. Seventy-two up- or down-regulated mRNAs were identified, including 36 novel sequences and those of cell cycle regulatory proteins (TGF-1beta2, Cyclin D1, p57Kip2), transcription factors (beta-catenin, Sox11, DP1), signaling proteins (SH3-domain binding protein, G-protein-coupled receptor, Ser-Thr protein kinase), cell adhesion molecules (syndecan-4, integrin-beta1), and also gene33, H19, SM20, IGFBP5, MAMA receptor, lectin, keratin, beta-tubulin, calreticulin , GRP78, ERp72, MnSoD, thioredoxin, and others. Some have previously been associated with kidney development and serve as good controls for expected changes, while most have not been linked with kidney epithelial cell differentiation. Using thin sections of embryonic kidney and labeled antisense RNA probes, we applied RNA hybridization to confirm the results of DD and related the expression of these genes to specific cell lineages of the developing kidney. These results provide a window into the events that mediate this critical differentiation process and suggest that a limited number of interrelated events direct the epithelial conversion of metanephric mesenchyme.

2/AB/29 (Item 3 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE
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01287595 1999265266
Regulation of the dolichol pathway in human fibroblasts by the endoplasmic reticulum unfolded protein response
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Journal: Proceedings of the National Academy of Sciences of the United States of America, 96/23 (13050-13055), 1999, United States
PUBLICATION DATE: November 9, 1999
CODEN: PNASA
ISSN: 0027-8424
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 50

Accumulation of unfolded proteins within the endoplasmic reticulum (ER) of eukaryotic cells triggers the unfolded protein response (UPR), which activates transcription of several genes encoding ER chaperones and folding enzymes. This study reports that conversion of dolichol-linked Maninf 2inf - $D5GlcNAcinf 2 intermediates into mature Glcinf 3Maninf 9GlcNAcinf 2 oligosaccharides in primary human adult dermal fibroblasts is also stimulated by the UPR. This stimulation was not evident in several immortal cell lines and did not require a cytoplasmic stress response. Inhibition of dolichol-linked Glcinf 3Maninf 9GlcNAcinf 2 synthesis by glucose deprivation could be counteracted by the UPR, improving the transfer of Glcinf 3Maninf 9GlcNAcinf 2 to asparagine residues on nascent polypeptides. Glycosidic processing of asparagine-linked Glcinf 3Maninf 9GlcNAcinf 2 in the ER leads to the production of monoglucosylated oligosaccharides that promote nteraction with the lectin chaperones calreticulin and calnexin.

Thus, control of the dolichol-linked Glcinf 3Maninf 9GlcNAcinf 2 supply gives the UPR the potential to maintain efficient protein folding in the ER without new synthesis of chaperones or folding enzymes.

2/AB/30 (Item 4 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE
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00456930 96150870
Geranylgeraniol causes a decrease in levels of calreticulin and tyrosine phosphorylation of a 36-kDa protein prior to the appearance of apoptotic features in HL-60 cells
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ADDRESS: S. Nakajo, Laboratory of Biological Chemistry, School of Pharmaceutical Sciences, Showa University, 1-5-8 Hatanodai, Shinagawa-ku, Tokyo 142, Japan
Journal: Biochemical and Biophysical Research Communications, 226/3 (741-745), 1996, United States
PUBLICATION DATE: 19960000
CODEN: BBRCA
ISSN: 0006-291X
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English

It was demonstrated recently that geranylgeraniol (GGO) has potent apoptosis-inducing activity in various lines of tumor cells, including HL-60 cells. In the present study, we found that GGO markedly inhibited the expression of a calcium-binding protein, calreticulin , prior to the induction of apoptosis in HL-60 cells. Furthermore, we also observed a significant decrease in the tyrosine phosphorylation of a 36-kDa protein that is a major tyrosine-phosphorylated protein in HL-60 cells. These findings suggest that decreases in levels of calreticulin and in the tyrosine phosphorylation of the 36-kDa protein might be associated with the induction of apoptosis by GGO in HL-60 cells.

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DIALOG(R)File 71:ELSEVIER BIOBASE
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00417447 96111241
Association of 1alpha,25-dihydroxyvitamin Dinf 3-occupied vitamin D receptors with cellular membrane acceptance sites
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Journal: Endocrinology, 137/9 (3649-3658), 1996, United States
PUBLICATION DATE: 19960000
CODEN: ENDOA
ISSN: 0013-7227
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English

We previously reported nongenomic activation of ROS 17/2.8 cells by vitamin D metabolites (1alpha,25-dihydroxyvitamin Dinf 3 (1alpha,25(OH)inf 2Dinf 3), 25- hydroxyvitamin Dinf 3, 22-oxa-calcitriol, etc.). The hormone 1alpha,25-(OH)inf 2Dinf 3, or calcitriol, mediated rapid transient changes in intracellular free calcium levels and concomitant stimulation of inositol polyphosphate and diacylglycerol production. These effects resemble the mechanism of cell activation induced by ligands with plasma

membrane (PM) receptors. As preliminary studies indicated that PM isolated from ROS 17/2.8 cells lacked specific binding sites for calcitriol alone, we studied the association between calcitriol-occupied vitamin D receptors (VDR) and ROS 17/2.8 cellular membranes. Saturable binding to the PM and the endoplasmic reticulum (ER) of calcitriol-occupied VDR was demonstrated. Binding of the VDR-(sup 3H)calcitriol complex was displaceable by nonradioactive VDR/calcitriol, but not by the unoccupied VDR or by calcitriol alone. ER binding, but not PM binding, was competitively inhibited by a peptide from the VDR sequence recognized by an ER protein, calreticulin , and by an anticalreticulin antibody. The monoclonal antibody (9A7) against the VDR inhibited PM and ER binding of the hormone- occupied VDR. These results were substantiated by studies using baculovirus-expressed human VDR for binding studies with the PM and ER and for immunoblot analysis. We conclude that specific PM and ER sites of association for calcitriol-occupied VDR exist and suggest that these associations could participate in the nongenomic rapid actions of 1alpha,25-(OH)inf 2Dinf 3.

2/AB/32 (Item 6 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE
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00335786 96006242
The mitogenic effects of the Bbeta chain of fibrinogen are mediated through cell surface calreticulin
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ADDRESS: A.J. Gray, United Kingdom
Journal: Journal of Biological Chemistry, 270/44 (26602-26606), 1995
PUBLICATION DATE: 19950000
CODEN: JBCHA
ISSN: 0021-9258
DOCUMENT TYPE: Article
LANGUAGES: English

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DIALOG(R)File 71:ELSEVIER BIOBASE
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00006409 94015505
Calcium uptake during mitogenic stimulation of human lymphocytes: Characterization of intracellular calcium compartments and demonstration of the presence of immunoreactive calrecticulin
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ADDRESS: M. Michalak, Cardiovascular Disease Res. Group, Department of Pediatrics, University of Alberta, Edmonton, Alta., Canada
Journal: Immunological Investigations, 22/6-7 (415-429), 1993, United States
PUBLICATION DATE: 19930000
CODEN: IMINE
ISSN: 0882-0139
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English

Phytohemagglutinin (PHA) stimulation of human peripheral blood lymphocytes (HPBL) rapidly increases sup 4sup 5Casup 2sup + uptake into intracellular pools. Detectable increase in sup 4sup 5Casup 2sup + uptake occurred only on exposure to mitogenic lectins but not with non-mitogenic lectins. However, intracellular free Casup 2sup + concentration ((Casup 2sup +)i)

increased comparably on exposure to either mitogenic or non-mitogenic lectins. Permeabilization of sup 4sup 5Casup 2sup + loaded cells revealed distinct pools of Casup 2sup + uptake. The highly digitonin sensitive pool I (permeabilized by 0.02% digitonin) exchanged slowly and included a part that represented endoplasmic reticulum. Pool II was defined by lower digitonin sensitivity, had a much faster initial uptake. Pool III was digitonin-resistant and predominantly non-vesicular. During the first 120 min of PHA stimulation, significant increase in sup 4sup 5Casup 2sup + uptake occurred only into pool II. Progressive increase in uptake into pool I then occurred so that by 24 hours, this pool constituted the major fraction of PHA induced increment in total sup 4sup 5Casup 2sup + uptake. Using specific antibody to the calcium binding protein calreticulin , an analogous immunoreactive protein was detectable in resting HPBL. PHA stimulation led to a striking increase in abundance of immunoreactive calreticulin so that 24 hrs after PHA stimulation, there was a 28 and 3.4 fold increase in the amount of immunoreactive calreticulin present in the non-particulate fraction and the total particulate membrane fraction, respectively. A major part (72%) of the total cellular immunoreactive calreticulin in PHA stimulated cells at 24 hrs was released into the medium after permeabilization of lymphocytes with 0.02% digitonin, corresponding to the location of calcium uptake pool I.

2/AB/34 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE
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11104731 EMBASE No: 2001125071
Unliganded and liganded estrogen receptors protect against cancer invasion via different mechanisms
Platet N.; Cunat S.; Chalbos D.; Rochefort H.; Garcia M.
Dr. M. Garcia, Unite 540 INSERM, 60, rue de Navacelles, 34090 Montpellier France
AUTHOR EMAIL: garcia@u540.montp.inserm.fr
Molecular Endocrinology (MOL. ENDOCRINOL.) (United States) 2000, 14/7 (999-1009)
CODEN: MOENE ISSN: 0888-8809
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 50

While estrogens are mitogenic in breast cancer cells, the presence of estrogen receptor alpha (ERalpha) clinically indicates a favorable prognosis in breast carcinoma. To improve our understanding of ERalpha action in breast cancer, we used an original in vitro method, which combines transient transfection and Matrigel invasion assays to examine its effects on cell invasiveness. ERalpha expression in MDA-MB-231 breast cancer cells reduced their invasiveness by 3-fold in the absence of hormone and by 7-fold in its presence. Integrity of hormone and DNA-binding domains and activating function 2 were required for estradiol-induced inhibition, suggesting that transcriptional activation of estrogen target genes was involved. In contrast, these domains were dispensable for hormone-independent inhibition. Analysis of deletion mutants of ERalpha indicated that amino acids 179-215, containing the N-terminal zinc finger of the DNA-binding domain, were required for ligand-independent receptor action. Among different members of the nuclear receptor family, only unliganded ERalpha and ERbeta reduced invasion. Calreticulin , a CaSUP2+-binding protein that could interact with amino acids 206-211 of ERalpha, reversed hormone-independent ERalpha inhibition of invasion. However, since calreticulin alone also inhibited invasion, we propose that this protein probably prevents ERalpha interaction with another

unidentified invasion-regulating factor. The inhibitor role of the unliganded ER was also suggested in three ERalpha-positive cell lines, where ERalpha content was inversely correlated with cell migration. We conclude that ERalpha protects against cancer invasion in its unliganded form, probably by protein-protein interactions with the N-terminal zinc finger region, and after hormone binding by activation of specific gene transcription.

2/AB/35 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE
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07908052 EMBASE No: 1999382009
Role of integrins in cancer: Survey of expression patterns
Mizejewski G.J.
G.J. Mizejewski, Division of Molecular Medicine, Wadsworth Center, New York State Department of Health, Empire State Plaza, Albany, NY 12201-0509 United States
Proceedings of the Society for Experimental Biology and Medicine (PROC. SOC. EXP. BIOL. MED.) (United States) 1999, 222/2 (124-138)
CODEN: PSEBA ISSN: 0037-9727
DOCUMENT TYPE: Journal; Short Survey
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 142

Tumor cells are characterized by uncontrolled growth, invasion to surrounding tissues, and metastatic spread to distant sites. Mortality from cancer is often due to metastasis since surgical removal of tumors can enhance and prolong survival. The integrins constitute a family of transmembrane receptor proteins composed of heterodimeric complexes of noncovalently linked alpha and beta chains. Integrins function in cell-to-cell and cell-to-extracellular matrix (ECM) adhesive interactions and transduce signals from the ECM to the cell interior and vice versa. Hence, the integrins mediate the ECM influence on cell growth and differentiation. Since these properties implicate integrin involvement in cell migration, invasion, intra- and extravasation, and platelet interaction, a role for integrins in tumor growth and metastasis is obvious. These findings are underpinned by observations that the integrins are linked to the actin cytoskeleton involving talin, vinculin, and alpha-actinin as intermediaries. Such cytoskeletal changes can be manifested by rounded cell morphology, which is often coincident with tumor transformation via decreased or increased integrin expression patterns. For the various types of cancers, different changes in integrin expression are further associated with tumor growth and metastasis. Tumor progression leading to metastasis appears to involve equipping cancer cells with the appropriate adhesive (integrin) phenotype for interaction with the ECM. Therapies directed at influencing integrin cell expression and function are presently being explored for inhibition of tumor growth , metastasis, and angiogenesis . Such therapeutic strategies include anti-integrin monoclonal antibodies, peptidic inhibitors (cyclic and linear), calcium-binding protein antagonists, proline analogs, apoptosis promotors, and antisense oligonucleotides. Moreover, platelet aggregation induced by tumor cells, which facilitates metastatic spread, can be inhibited by the disintegrins, a family of viper venom-like peptides. Therefore, adhesion molecules from the integrin family and components of angiogenesis might be useful as tumor progression markers for prognostic and for diagnostic purposes. Development of integrin cell expression profiles for individual tumors may have further potential in identifying a cell surface signature for a specific tumor type and/or stage. Thus, recent advances in elucidating the structure, function, ECM binding, and signaling pathways of

the integrins have led to new and exciting modalities for cancer therapeutics and diagnoses.

2/AB/36 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE
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06682238 EMBASE No: 1996347152
Identification by subtractive hybridization of a spectrum of novel and unexpected genes associated with in vitro differentiation of human cytotrophoblast cells
Morrish D.W.; Linetsky E.; Bhardwaj D.; Li H.; Dakour J.; Marsh R.G.; Paterson M.C.; Godbout R.
Perinatal Research Centre, University of Alberta, WW Cross Cancer Institute,Edmonton, Alta. T6G 2S2 Canada
Placenta (PLACENTA) (United Kingdom) 1996, 17/7 (431-441)
CODEN: PLACD ISSN: 0143-4004
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

We have previously demonstrated that epidermal growth factor (EGF), colony stimulating factor-1 (CSF-1), and granulocyte-monocyte colony stimulating factor (GMCSF) stimulate, while transforming growth factor beta1 (TGFbeta1) inhibits , cytotrophoblast differentiation. To identify genes mediating EGF-induced differentiation, we constructed a subtracted cDNA library between undifferentiated cytotrophoblast and differentiating cytotrophoblast. We identified six novel genes and four known syncytial products alpha-human chorionic gonadotrophin (alphahCG) pregnancy-specific beta1-glycoprotein, 3beta-hydroxysteroid dehydrogenase, and plasminogen activator inhibitor type 1 whose mRNAs increased during differentiation. Ten other genes were identified whose mRNAs increased during differentiation. Five of these (keratin 19, calcreticulin, heat shock protein 27, serum and glucocorticoid-regulated kinase and adrenomedullin) were not previously reported to be expressed in placenta. Five other genes known to be expressed in placenta were identified: keratin 8, fibronectin, mitochondrial ATP synthase, H19, and cytosolic copper-zinc superoxide dismutase (SOD-1). Several of these genes may have regulatory functions in trophoblast differentiation.

2/AB/37 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE
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06522465 EMBASE No: 1996187413
Genomic mechanisms involved in the pleiotropic actions of 1,25-dihydroxyvitamin Dinf 3
Christakos S.; Raval-Pandya M.; Wernyj R.P.; Yang W.
Dept. Biochemistry Molecular Biology, University of Medicine Dentistry NJ, New Jersey Medical School, 185 South Orange Avenue,Newark, NJ 07103-2714 United States
Biochemical Journal (BIOCHEM. J.) (United Kingdom) 1996, 316/2 (361-371)
CODEN: BIJOA ISSN: 0264-6021
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The biologically active metabolite of vitamin D (cholecalciferol), i.e. 1,25-dihydroxyvitamin Dinf 3 (1,25(OH)inf 2Dinf 3), is a secosteroid hormone whose mode of action involves stereospecific interaction with an

intracellular receptor protein (vitamin D receptor; VDR). 1,25(OH)inf 2Dinf 3 is known to be a principal regulator of calcium homeostasis, and it has numerous other physiological functions including inhibition of proliferation of cancer cells, effects on hormone secretion and suppression of T-cell proliferation and cytokine production. Although the exact mechanisms involved in mediating many of the different effects of 1,25(OH)inf 2Dinf 3 are not completely defined, genomic actions involving the VDR are clearly of major importance. Similar to other steroid receptors, the VDR is phosphorylated; however, the exact functional role of the phosphorylation of the VDR remains to be determined. The VDR has been reported to be regulated by 1,25(OH)inf 2Dinf 3 and also by activation of protein kinases A and C, suggesting co-operativity between signal transduction pathways and 1,25(OH)inf 2Dinf 3 action. The VDR binds to vitamin D-responsive elements (VDREs) in the 5' flanking region of target genes. It has been suggested that VDR homodimerization can occur upon binding to certain VDREs but that the VDR/retinoid X receptor (RXR) heterodimer is the functional transactivating species. Other factors reported to be involved in VDR-mediated transcription include chicken ovalbumin upstream promoter (COUP) transcription factor, which is involved in active silencing of transcription, and transcription factor IIB, which has been suggested to play a major role following VDR/RXR heterodimerization. Newly identified vitamin D-dependent target genes include those for Casup 2sup +/Mgsup 2sup +-ATPase in the intestine and p21 in the myelomonocytic U937 cell line. Elucidation of the mechanisms involved in the multiple actions of 1,25(OH)inf 2Dinf 3 will be an active area of future research.

2/AB/38 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal
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14998472 PASCAL No.: 01-0153819
Analysis of genes preferentially expressed in early stage of pollinated and parthenocarpic fruit in eggplant
NAGASAWA Masaki; SUGIYAMA Akira; MORI Hitoshi; SHIRATAKE Katsuhiro; YAMAKI Shohei
Graduate School of Bioagricultural Sciences, Nagoya University, Nagoya 464-8601, Japan
Journal: Journal of plant physiology, 2001, 158 (2) 235-240
Language: English
To isolate genes preferentially expressed at early stages of fruits in eggplant (Solanum melongena L., var. Senryo No. 2), subtractive hybridization was used on cDNAs from pollinated fruits and poly(A) SUP + RNA from unpollinated fruits at 3 days after anthesis. In this way, 8 cDNA clones were isolated from a cDNA library constructed from pollinated fruits at 3 days after anthesis, and were designated EEF13, 20, 22, 26, 38, 45, 48, and 53, respectively. Expression patterns of EEF genes in pollinated fruit were similar to those in 4-chlorophenoxyacetic acid (4-CPA)-treated fruit by Northern blot analyses. During development of pollinated and 4-CPA-treated fruit, the transcription patterns of EEF genes were classified into three types. EEF20 and EEF38 genes whose products are highly similar to histones, were expressed abundantly on the day of anthesis and continued to be expressed during the early stages of fruit development (Type 1). Transcription of five genes was at higher level from 2 to 4 days after anthesis (Type 2), and the encoded products of EEF22 and EEF26, showed high similarity with calreticulin and polyphenol oxidase, respectively. Another gene, EEF48 (Type 3), showed high and continuous expression from 2 to 20 days after anthesis and was almost restricted to fruits. Deduced amino acid sequence of EEF48 showed high similarity with a cell wall protein.

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2/AB/39 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal
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14876420 PASCAL No.: 01-0023802
Aluminum-induced 1 rightarrow 3- beta -D-glucan inhibits cell-to-cell trafficking of molecules through plasmodesmata. A new mechanism of aluminum toxicity in plants

SIVAGURU Mayandi; FUJIWARA Toru; SAMAJ Josef; BALUSKA Frantisek; ZHENMING YANG; OSAWA Hiroki; MAEDA Takanori; MORI Tomoko; VOLKMANN Dieter; MATSUMOTO Hideaki

Research Institute for Bioresources, Okayama University, Kurashiki 710-0046, Japan; Department of Applied Biological Chemistry, Graduate School of Agricultural and Life Sciences, University of Tokyo, Tokyo 113-8657, Japan; Precursory Research for Embryonic Science and Technology, Japan Science and Technology Corporation, JST, Chiba 263-1123, Japan; Department of Agronomy, Institute of Plant Genetics and Biotechnology, Slovak Academy of Sciences, 950, 07 Nitra, Slovakia; Department of Plant Cell Biology, Rheinische Friedrich-Wilhelms-Universitaet Bonn, 53115 Bonn, Germany; Changchun University of Agriculture and Animal Sciences, Changchun, 130062, China; Bio-Oriented Technology Research Advancement Institution, Omiya 331-8537, Japan

Journal: Plant physiology : (Bethesda), 2000, 124 (3) 991-1005
Language: English

Symplastic intercellular transport in plants is achieved by plasmodesmata (PD). These cytoplasmic channels are well known to interconnect plant cells to facilitate intercellular movement of water, nutrients, and signaling molecules including hormones. However, it is not known whether Al may affect this cell-to-cell transport process, which is a critical feature for roots as organs of nutrient/water uptake. We have microinjected the dye lucifer yellow carbohydrazide into peripheral root cells of an Al-sensitive wheat (Triticum, aestivum cv Scout 66) either before or after Al treatment and followed the cell-to-cell dye-coupling through PD. Here we show that the Al-induced root growth inhibition is closely associated with the Al-induced blockage of cell-to-cell dye coupling. Immunofluorescence combined with immuno-electron microscopic techniques using monoclonal antibodies against 1 rightarrow 3- beta -D-glucan (callose) revealed circumstantial evidence that Al-induced callose deposition at PD may responsible for this blockage of symplastic transport. Use of 2-deoxy-D-glucose, a callose synthesis inhibitor, allowed us to demonstrate that a reduction in callose particles correlated well with the improved dye-coupling and reduced root growth inhibition . While assessing the tissue specificity of this Al effect, comparable responses were obtained from the dye-coupling pattern in tobacco (Nicotiana tabacum) mesophyll cells. Analyses of the Al-induced expression of PD-associated proteins, such as calreticulin and unconventional myosin VIII, showed enhanced fluorescence and co-localizations with callose deposits. These results suggest that Al-signal mediated localized alterations to calcium homeostasis may drive callose formation and PD closure. Our data demonstrate that extracellular Al-induced callose deposition at PD could effectively block symplastic transport and communication in higher plants.

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2/AB/40 (Item 3 from file: 144)
DIALOG(R)File 144:Pascal

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14782444 PASCAL No.: 00-0462151
Effective targeting of tumor vasculature by the angiogenesis inhibitors vasostatin and interleukin-12
LEI YAO; PIKE S E; SETSUDA J; PAREKH J; GUPTA G; RAFFELD M; JAFFE E S; TOSATO G
Medicine Branch, National Cancer Institute, Division of Clinical Sciences, National Institutes of Health, Bethesda, MD, United States; Center for Biologics Evaluation and Research, Rockville, MD, United States; Laboratory of Pathology, National Cancer Institute, Division of Clinical Science, National Institutes of Health, Bethesda, MD, United States
Journal: Blood, 2000, 96 (5) 1900-1905
Language: English
Solid tumors are dependent on preexisting vasculature and neovascularization for their growth. Successful cancer therapies targeting the tumor vasculature would be expected to block the existing tumor blood supply and to prevent tumor neovascularization. We tested the antitumor activity of experimental therapy with 2 distinct antiangiogenic drugs. Vasostatin inhibits endothelial cell growth and neovascularization, and interleukin-12 (IL-12) targets the tumor vasculature acting through Interferon- gamma (IFN-y) and the downstream chemokines interferon-inducible protein-10 (IP-10) and monokine induced by IFN- gamma . Individually, vasostatin and IL-12 produced distinct efficacy profiles in trials aimed at reducing tumor growth in athymic mice. In combination, these inhibitors halted the growth of human Burkitt lymphoma, colon carcinoma, and ovarian carcinoma. Thus, cancer therapy that combines distinct Inhibitors of angiogenesis is a novel, effective strategy for the experimental treatment of cancer .

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2/AB/41 (Item 1 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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01824278 SUPPLIER NUMBER: 54149371 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Vasostatin Inhibits Angiogenesis.
Cancer Weekly Plus, NA
March 15,
1999
PUBLICATION FORMAT: Newsletter LANGUAGE: English RECORD TYPE: Fulltext
TARGET AUDIENCE: Professional
WORD COUNT: 185 LINE COUNT: 00020

2/AB/42 (Item 1 from file: 342)
DIALOG(R)File 342:Derwent Patents Citation Indx
(c) 2001 Derwent Info Ltd. All rts. reserv.

04258969 WPI Acc No: 00-303767/26
Inhibiting endothelial cell growth and angiogenesis using calreticulin, useful for suppressing tumor growth -
Patent Assignee: (USSH) US DEPT HEALTH & HUMAN SERVICES
Author (Inventor): TOSATO G; PIKE S E; YAO L
Patent (basic)
Patent No Kind Date Examiner Field of Search
WO 200020577 A1 000413 (BASIC)
Derwent Week (Basic): 0026
Priority Data: US 103438 (981006)

Applications: AU 9962917 (991005); WO 99US23240 (991005)
Designated States
(National): AE; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CR; CU; CZ; DE; DK; DM; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN ; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR ; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZW
(Regional): AT; BE; CH; CY; DE; DK; EA; ES; FI; FR; GB; GH; GM; GR; IE; IT; KE; LS; LU; MC; MW; NL; OA; PT; SD; SE; SL; SZ; TZ; UG; ZW
Derwent Class: B04; D16
Int Pat Class: A61K-038/17; C07K-014/47
Number of Patents: 002
Number of Countries: 089
Number of Cited Patents: 005
Number of Cited Literature References: 005
Number of Citing Patents: 000

2/AB/43 (Item 2 from file: 342)
DIALOG(R)File 342:Derwent Patents Citation Indx
(c) 2001 Derwent Info Ltd. All rts. reserv.

04252529 WPI Acc No: 96-443637/45
Prod. comprising calreticulin or calreticulin-binding peptide - useful for modulating hormone responsiveness, esp. for treating e.g. cancer, osteoporosis or arthritis
Patent Assignee: (DEDH/) DEDHAR S
Author (Inventor): DEDHAR S
Patent (basic)

Patent No	Kind	Date	Examiner Field of Search
CA 2140814	A	960724 (BASIC)	

Derwent Week (Basic): 9645
Priority Data: CA 2140814 (950123)
Applications: CA 2140814 (950123)
Derwent Class: B04; D16
Int Pat Class: A61K-038/17; C07K-014/435
Number of Patents: 001
Number of Countries: 001
Number of Cited Patents: 000
Number of Cited Literature References: 000
Number of Citing Patents: 000

2/AB/44 (Item 3 from file: 342)
DIALOG(R)File 342:Derwent Patents Citation Indx
(c) 2001 Derwent Info Ltd. All rts. reserv.

04227579 WPI Acc No: 00-558368/51
Eliciting immune response in vertebrate for prevention and treatment of cancer and infectious diseases involves administering purified complex comprising calreticulin bound to an antigenic molecule -
Patent Assignee: (UYDU-) UNIV DUKE
Author (Inventor): GILBOA E; NAIR S K; NICCHITTA C V
Patent (basic)

Patent No	Kind	Date	Examiner Field of Search
WO 200050080	A1	000831 (BASIC)	

Derwent Week (Basic): 0051
Priority Data: US 261473 (990226)
Applications: AU 200032414 (000223); WO 2000US4565 (000223)
Designated States
(National): AE; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CR;

CU; CZ; DE; DK; DM; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN ; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM ; TR; TT; TZ; UA; UG; UZ; VN; YU; ZA; ZW
(Regional): AT; BE; CH; CY; DE; DK; EA; ES; FI; FR; GB; GH; GM; GR; IE; IT; KE; LS; LU; MC; MW; NL; OA; PT; SD; SE; SL; SZ; TZ; UG; ZW
Derwent Class: B04
Int Pat Class: A01N-037/18; A61K-039/395
Number of Patents: 002
Number of Countries: 089
Number of Cited Patents: 000
Number of Cited Literature References: 001
Number of Citing Patents: 000

2/AB/45 (Item 4 from file: 342)
DIALOG(R)File 342:Derwent Patents Citation Indx
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03414773 WPI Acc No: 99-142854/12
New peptides that bind calreticulin and modulate gene expression - are activated by hormone receptors, useful in the treatment of cancer, chronic inflammation and osteoporosis
Patent Assignee: (DEDH/) DEDHAR S; (DOER/) DOERSEN C W; (MAZU/) MAZUR A W
Author (Inventor): DEDHAR S; DOERSEN C W; MAZUR A W
Patent (basic)

Patent No	Kind	Date	Examiner	Field of Search
WO 9905172	A2	990204 (BASIC)		

Derwent Week (Basic): 9912
Priority Data: US 900241 (970724)
Applications: AU 9885251 (980724); WO 98CA715 (980724)
Designated States
(National): AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU; CZ; DE; DK; EE; ES; FI; GB; GE; GH; GM; HR; HU; ID; IL; IS; JP; KE; KG; KP ; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; US; UZ ; VN; YU; ZW
(Regional): AT; BE; CH; CY; DE; DK; EA; ES; FI; FR; GB; GH; GM; GR; IE; IT; KE; LS; LU; MC; MW; NL; OA; PT; SD; SE; SZ; UG; ZW
Derwent Class: B04
Int Pat Class: A61K-038/08; A61K-038/17; C07K-007/06; C07K-007/08
Number of Patents: 002
Number of Countries: 082
Number of Cited Patents: 003
Number of Cited Literature References: 002
Number of Citing Patents: 000

2/AB/46 (Item 5 from file: 342)
DIALOG(R)File 342:Derwent Patents Citation Indx
(c) 2001 Derwent Info Ltd. All rts. reserv.

02647753 WPI Acc No: 96-362634/36
Cpds esp. calreticulin, its mimetics or binding peptides for modulating hormone responsiveness - and treating diseases, e.g. cancer, by regulating hormone-induced gene transcription.
Patent Assignee: (DEDH/) DEDHAR S; (STAR/) ST-ARNAUD R
Author (Inventor): DEDHAR S; ST-ARNAUD R
Patent (basic)

Patent No	Kind	Date	Examiner	Field of Search
WO 9623001	A1	960801 (BASIC)		A61K; C07K; C12N

Derwent Week (Basic): 9636
Priority Data: US 377432 (950124)
Applications: US 377432 (950124); AU 9539203 (951123); EP 95936911 (951123); WO 95CA664 (951123); JP 96522508 (951123); KR 97705041 (970724); AU 9945861 (990901)
Designated States
(National): AL; AM; AT; AU; BB; BG; BR; BY; CA; CH; CN; CZ; DE; DK; EE; ES; FI; GB; GE; HU; IS; JP; KE; KG; KP; KR; KZ; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; TJ; TM; TT; UA; UG; US; UZ; VN
(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; KE; LS; LU; MC; MW; NL; OA; PT; SD; SE; SZ; UG
Derwent Class: B04; D16
Int Pat Class: A61K-038/04; A61K-038/22; A61K-045/00; A61K-048/00; A61P-019/02; A61P-019/08; A61P-035/00; C07K-007/04; C07K-007/06; C07K-014/47; C07K-014/575; C07K-014/5751; C12N-015/09
Number of Patents: 007
Number of Countries: 067
Number of Cited Patents: 005
Number of Cited Literature References: 163
Number of Citing Patents: 001

2/AB/47 (Item 1 from file: 345)
DIALOG(R)File 345:Inpadoc/Fam.& Legal Stat
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15905845
Basic Patent (No,Kind,Date): WO 200020577 A1 20000413 <No. of Patents: 002>
USE OF CALRETICULIN AND CALRETICULIN FRAGMENTS TO INHIBIT ENDOTHELIAL CELL GROWTH AND ANGIOGENESIS, AND SUPPRESS TUMOR GROWTH (English)
Patent Assignee: US HEALTH (US); TOSATO GIOVANNA (US); PIKE SANDRA E (US); YAO LEI (US)
Author (Inventor): TOSATO GIOVANNA (US); PIKE SANDRA E (US); YAO LEI (US)
Designated States : (National) AE; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CR; CU; CZ; DE; DK; DM; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZW (Regional) GH; GM; KE; LS; MW; SD; SL; SZ; TZ; UG; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG
Filing Details: WO 130000 With international search report; Before expiration of time limit for amending the claims and to be republished in the event of the receipt of the amendments
IPC: *C12N-015/11; C07K-014/47; A61K-038/17
Derwent WPI Acc No: *C 00-303767; C 00-303767
Language of Document: English
Patent Family:

Patent No	Kind	Date	Applic No	Kind	Date	
AU 9962917	A1	20000426	AU 9962917	A	19991005	
WO 200020577	A1	20000413	WO 99US23240	A	19991005	(BASIC)

Priority Data (No,Kind,Date):
US 103438 P 19981006
WO 99US23240 W 19991005

2/AB/48 (Item 2 from file: 345)
DIALOG(R)File 345:Inpadoc/Fam.& Legal Stat
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13143327
Basic Patent (No,Kind,Date): CA 2140814 AA 960724 <No. of Patents: 001>
USE OF CALRETICULIN IN MODULATING HORMONE RESPONSIVENESS AND NEW PHARMACEUTICALS FOR TREATING CANCER, OSTEOPOROSIS AND CHRONIC INFLAMMATORY DISEASE (English; French)
Patent Assignee: DEDHAR SHOUKAT (CA)
Author (Inventor): DEDHAR SHOUKAT (CA)
IPC: *C12N-015/12; C07K-014/435; A61K-038/17
CA Abstract No: 125(16)204501Y
Derwent WPI Acc No: C 96-443637
Language of Document: English
Patent Family:

Patent No	Kind	Date	Applic No	Kind	Date	
CA 2140814	AA	960724	CA 2140814	A	950123	(BASIC)

Priority Data (No,Kind,Date):
CA 2140814 A 950123

2/AB/49 (Item 1 from file: 351)
DIALOG(R)File 351:Derwent WPI
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013973293
WPI Acc No: 2001-457506/200149
XRAM Acc No: C01-138372
Pharmaceutical composition, used to treat or prevent infection or cancer, comprises a complex comprising a heat shock protein-binding fragment associated with a molecule displaying antigenicity of an infectious agent or cancer cell
Patent Assignee: UNIV CONNECTICUT HEALTH CENT (UYCO-N)
Inventor: SRIVASTAVA P K
Number of Countries: 022 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200152791	A2	20010726	WO 2001US1781	A	20010118	200149	B

Priority Applications (No Type Date): US 2000488393 A 20000120
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200152791	A2	E	106	A61K-000/00	

Designated States (National): AU CA JP
Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR

Abstract (Basic): WO 200152791 A2
Abstract (Basic):
NOVELTY - A novel pharmaceutical composition (I) comprises a molecular complex which comprises a heat shock protein (hsp) peptide-binding fragment (BF) noncovalently associated with an antigenic molecule (AM) displaying antigenicity of an infectious agent or cancer cell antigen, where the binding fragment comprises a peptide-binding domain (BD).
DETAILED DESCRIPTION - The peptide-binding domain in (I) is contiguous on the N-terminal side with x number of amino acids (aas) that naturally flank the binding domain on the N-terminal side, and contiguous on the C-terminal side with y number of aas that naturally flank the binding domain on the C-terminal side. x plus y is not more than 400.
INDEPENDENT CLAIMS are also included for the following:
(1) a recombinant cell (II) infected with a pathogen and

transformed with a nucleic acid (NA) comprising a nucleotide (nt) sequence that is operably linked to a promoter and which encodes an hsp peptide BF comprising BD, where the BF noncovalently associates with an AM to form a complex which can elicit an immune response to AM;

(2) a recombinant cancer cell (III) transformed with an NA comprising a nt sequence that is operably linked to a promoter and which encodes a hsp peptide BF comprising BD, where the BF noncovalently associates with an AM to form a complex which can elicit an immune response to AM;

(3) a recombinant cell (IV) transformed with an NA comprising a nt sequence that is operably linked to a promoter and which encodes an hsp peptide BF comprising BD, and another NA comprising another nt sequence that is operably linked to a promoter and which encodes an AM, where the BF and the AM are expressed in the cell and noncovalently associate to form a complex which can elicit an immune response to AM;

(4) preparing (M1) a complex of an hsp peptide BF noncovalently associated with a peptide, where BF comprises BD, comprising culturing cells transformed with a NA comprising a nt sequence that is operably linked to a promoter and which encodes BF, where the BF is expressed by the cells and associates with peptides of the cells, and recovering the complexes of BF noncovalently associated with the peptides from the cells;

(5) preparing (M2) a complex of an hsp peptide BF noncovalently associated with a peptide, where BF comprises BD, comprising digesting hsps with a protease to form hsp peptide BFs, and contacting them with peptides to form complexes;

(6) eliciting (M3) an immune response against an antigen, comprising administering an immunogenic complex of an hsp peptide BF noncovalently associated with an AM displaying antigenicity of the antigen, where the hsp peptide BF comprises a BD that is contiguous on the N-terminal side with x number of amino acids (aas) that naturally flank the binding domain on the N-terminal side, and contiguous on the C-terminal side with y number of aas that naturally flank the binding domain on the C-terminal side. x plus y is not more than 400;

(7) treating or preventing (M4) an infectious disease or cancer comprising administering an immunogenic complex of an hsp peptide BF noncovalently associated with an AM displaying antigenicity of the infectious disease or of the cancer/metastasis type, or, when the disease is cancer the complex is obtained by recovering complexes from the cancer cells or their metastasis that recombinantly express the hsp peptide BF; and

(8) preparing (M6) a complex of an hsp peptide BF noncovalently associated with a peptide, where BF comprises BD, comprising digesting hsps noncovalently associated with peptides with a protease to form hsp peptide BFs noncovalently associated with peptides and;

(9) preparing (M7) in vitro complexes of hsp peptide BFs noncovalently associated with peptides, where BFs comprises BD, comprising incubating an hsp peptide BF and one or more AMs to form the complexes.

ACTIVITY - Cytostatic; antibacterial; antifungal; antiviral; immunostimulant.

No biological data given.

MECHANISM OF ACTION - Vaccine.

No details given.

USE - (I) is used for the treatment or prevention of an infectious disease or cancer (claimed).

pp; 106 DwgNo 0/3

2/AB/50 (Item 2 from file: 351)
DIALOG(R)File 351:Derwent WPI

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013628472
WPI Acc No: 2001-112680/200112
XRAM Acc No: C01-033610
Increasing the muscle mass of animals used in meat production by down regulating growth differentiation factor 8 (GDF-8) activity in the animal through induction of anti-GDF-8 antibody production
Patent Assignee: M & E BIOTECH AS (MEBI-N)
Inventor: HALKIER T; KLYSNER S; MOURITSEN S
Number of Countries: 094 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200105820	A2	20010125	WO 2000DK413	A	20000720	200112	B
AU 200059675	A	20010205	AU 200059675	A	20000720	200128	

Priority Applications (No Type Date): US 99145275 A 19990726; DK 991014 A 19990720
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200105820	A2	E	110	C07K-014/00	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW

AU 200059675	A		C07K-014/00	Based on patent WO 200105820

Abstract (Basic): WO 200105820 A2
Abstract (Basic):
NOVELTY - In vivo down regulation of growth differentiation factor 8 (GDF-8) activity in an animal, including a human, comprises presentation of a GDF-8 polypeptide or subsequence or GDF-8 analogue with a modified amino acid sequence to the immune system of the animal which induces production of anti-GDF-8 antibodies.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a GDF-8 analogue derived from an animal GDF-8 polypeptide which has a modification so that it induces production of anti-GDF-8 antibodies when used to immunize an animal;
(2) a nucleic acid (I) encoding the GDF-8 analogue of (1);
(3) a vector carrying (I) capable of autonomous replication;
(4) a transformed cell carrying the vector of (3) capable of replicating (I);
(5) a stable cell line carrying the vector of (3) that expresses (I) and optionally secretes on carries the GDF-8 analogue on its surface;
(6) preparation of the cell of (4);
(7) method for identifying a modified GDF-8 polypeptide capable of inducing antibodies against unmodified GDF-8 (self-protein) in an animal comprising preparing a set of mutually distinct modified GDF-8 polypeptides which have amino acid (aa) insertions, deletions or substitutions giving aa sequences containing foreign T-cell epitopes, testing members of the set for their ability to induce production of antibodies by the animal against unmodified GDF-8 and isolating members of the set which are able to induce this antibody production; and
(8) method for preparing an immunogenic composition which contains at least one modified GDF-8 polypeptide capable of inducing antibodies against unmodified GDF-8 (self-protein) in an animal.
ACTIVITY - Cardiant; immunomodulator.

No biological data is given.

MECHANISM OF ACTION - Vaccine.

USE - Down-regulation of GDF-8 activity is used to increase muscle mass in animals at least 5% when compared with animals with normal GDF-8 activity and up to at least 45% (claimed).

The method increases muscle mass in animals such as cows, pigs and poultry which are used for meat production. The down-regulation of GDF-8 activity is used to stimulate growth of skeletal muscle mass in animals. Anti-GDF8 vaccines can be used to treat human diseases such as cancer cachexia where muscle atrophy is pronounced and for patients suffering from acute and chronic heart failure.

ADVANTAGE - Using this method to increase muscle mass removes the need for extensive use of antibiotics in farm animals which can induce cross resistance towards human antibiotics in microorganisms pathogenic in man. Antibiotics only obtain a low growth rate but up to at least 45% increase in muscle mass is achieved with the new method. Growth hormones have also been used in the prior art but these are expensive and have the potential of the presence of residual hormones in meat. The treatment can be reserved for animals which are predestined for slaughter. The treatment should only require 1-4 annual injections but using growth hormones and antibiotics required more frequent administration.

pp; 110 DwgNo 0/5

2/AB/51 (Item 3 from file: 351)
DIALOG(R)File 351:Derwent WPI
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013475260
WPI Acc No: 2000-647203/200062
XRAM Acc No: C00-195762

Novel composition comprising at least 1 megakaryocyte and at least 1 compound that donates, transfers or releases nitric oxide, useful for the treatment of blood disorders such as thrombocytopenia, thrombocythemia or thrombocytopathy

Patent Assignee: UNIV BOSTON (UYBO-N)
Inventor: BATTINELLI E M; LOSCALZO J
Number of Countries: 092 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200057891	A1	20001005	WO 2000US6436	A	20000330	200062	B
AU 200038778	A	20001016	AU 200038778	A	20000330	200106	

Priority Applications (No Type Date): US 99126854 A 19990330
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200057891	A1	E	50	A61K-033/00	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

AU 200038778 A A61K-033/00 Based on patent WO 200057891

Abstract (Basic): WO 200057891 A1

Abstract (Basic):

NOVELTY - Composition comprising at least 1 megakaryocyte (I) and at least 1 compound (II) or its salt that donates, transfers or releases nitric oxide, or induces the production of endogenous nitric

oxide or endothelium-derived relaxing factor or is a substrate for nitric oxide synthase, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are provided for:

(1) a method of producing platelets or proplatelets in vitro comprising adding the composition to at least 1 megakaryocyte in culture;

(2) a method of producing platelets or proplatelets in vivo in a patient comprising administration of the composition to the patient;

(3) a method of treating or preventing a blood platelet disorder in a patient comprising administration of the composition to the patient;

(4) a method of decreasing platelet counts in a patient comprising administration of at least one compound that inhibits production of nitric oxide synthase; and

(5) a method of treating or preventing a blood platelet disorder in a patient, comprising:

(a) providing at least one megakaryocyte in culture;

(b) adding at least one compound (II) to (a) to produce platelets and/or proplatelets; and

(c) administering the platelets and/or proplatelets to the patient.

ACTIVITY - Hemostatic.

No biological data is given.

MECHANISM OF ACTION - Nitric oxide synthase production inhibition.

USE - The composition is used to treat blood disorders such as thrombocytopenia, thrombocythemia or thrombocytopathy (claimed)

pp; 50 DwgNo 0/2

2/AB/52 (Item 4 from file: 351)
DIALOG(R)File 351:Derwent WPI
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013386430
WPI Acc No: 2000-558368/200051
XRAM Acc No: C00-166328
Eliciting immune response in vertebrate for prevention and treatment of cancer and infectious diseases involves administering purified complex comprising calreticulin bound to an antigenic molecule
Patent Assignee: UNIV DUKE (UYDU-N)
Inventor: GILBOA E; NAIR S K; NICCHITTA C V
Number of Countries: 089 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200050080	A1	20000831	WO 2000US4565	A	20000223	200051	B
AU 200032414	A	20000914	AU 200032414	A	20000223	200063	

Priority Applications (No Type Date): US 99261473 A 19990226
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200050080	A1	E	82	A61K-039/395	

Designated States (National): AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

AU 200032414	A	A61K-039/395	Based on patent WO 200050080	

Abstract (Basic): WO 200050080 A1
Abstract (Basic):

NOVELTY - Eliciting (I) an immune response in a vertebrate, comprises administering a composition comprising a purified complex (C)

comprising calreticulin bound to an antigenic molecule; or an immunogenic amount of sensitized antigen presenting cells which are sensitized in vitro with the complex (C).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method of treating or preventing a type of cancer or an infectious disease in a vertebrate comprising the administration of a purified complex comprising calreticulin bound to an antigenic molecule specific to the type of cancer or infectious disease;

(2) a method of treating or preventing a type of cancer or an infectious disease in a vertebrate comprising the administration of sensitized antigen presenting cells having been sensitized in vitro with a complex comprising calreticulin and bound to an antigenic molecule specific to the type of cancer or infectious disease;

(3) a purified and isolated complex (II) comprising calreticulin non-covalently bound to an antigenic molecule;

(4) a pharmaceutical composition comprising (II) or an immunogenic amount of sensitized antigen presenting cells which are sensitized in vitro with (II);

(5) preparing (III) an immunogenic composition for inducing an immune response in a vertebrate, comprising:

(a) harvesting from an eukaryotic cell an immunogenic complex comprising calreticulin non-covalently bound to an antigen molecule which is capable of initiating an immune response in the vertebrate and combining the complex with a pharmaceutically acceptable carrier;

(b) reconstituting in vitro an antigenic molecule and calreticulin molecule to produce an immunogenic complex and combining the complex with a pharmaceutically acceptable carrier; or

(c) sensitizing antigen presenting cell in vitro with (II) and combining the antigenic presenting cell with pharmaceutically acceptable carrier; and

(6) a product produced by (III).

ACTIVITY - Cytostatic; virucide; hepatotropic; antiinflammatory; antibacterial; protozoacide; fungicide.

MECHANISM OF ACTION - Vaccine. The capacity of calreticulin to elicit cytotoxic T lymphocyte(s) (CTL) response in vivo was investigated in B16/F10.9 melanoma model systems. Endoplasmic reticulum chaperones GRP94 (ER paralog of the heat shock protein hsp90 family of chaperones), BiP (ER hsp70 homolog), ERp72, protein disulfide isomerase (PDI) and calreticulin were purified from an F10.9 tumor-derived microsomal fraction and control proteins were purified from a normal spleen-derived microsomal fraction. Mice were immunized twice intravenously at 14 days intervals with 10 microg of hsp. Splenocytes were isolated from the immunized mice 10 days after the last immunization and were restimulated in vitro with irradiated interferon-gamma pretreated F10.9 cells, and CTL activity was assayed subsequently against F10.9 (H2-Kb), EL4 (H2-Kb), or BALB/3T3 (H2-Kd) cells. Immunization with F10.9-derived calreticulin or GRP94 elicited a significant CTL response and the maximum level of CTL lysis was observed. Control target cells, EL4 and BALB/3T3, exhibited no lysis.

USE - Eliciting an immune response is useful for prevention and treatment of cancer and infectious disease in a vertebrate especially human.

pp; 82 DwgNo 0/0

2/AB/53 (Item 5 from file: 351)
DIALOG(R)File 351:Derwent WPI
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013178044

WPI Acc No: 2000-349917/200030
XRAM Acc No: C00-106406
Inducing immune responses to weakly immunogenic, tumor associated peptide antigens for the treatment of breast and prostate cancer
Patent Assignee: M & E BIOTECH AS (MEBI-N)
Inventor: DALUM I; GAUTAM A; HAANING J; KARLSSON G; LEACH D; MOURITSEN S; NIELSEN K G; RASMUSSEN BIRK P; STEINAA L; RASMUSSEN P B; BIRK P
Number of Countries: 090 Number of Patents: 004
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200020027	A2	20000413	WO 99DK525	A	19991005	200030	B
AU 9958510	A	20000426	AU 9958510	A	19991005	200036	
NO 200101586	A	20010531	WO 99DK525	A	19991005	200138	
			NO 20011586	A	20010328		
EP 1117421	A2	20010725	EP 99945967	A	19991005	200143	
			WO 99DK525	A	19991005		

Priority Applications (No Type Date): US 98105011 A 19981020; DK 981261 A 19981005; DK 9812 A 19981005
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200020027	A2	E	219	A61K-039/00	

Designated States (National): AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

AU 9958510	A		A61K-039/00	Based on patent WO 200020027
NO 200101586	A		A61K-000/00	
EP 1117421	A2	E	A61K-038/17	Based on patent WO 200020027

Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL RO SI

Abstract (Basic): WO 200020027 A2
Abstract (Basic):
NOVELTY - A method (I) for inducing immune responses against weakly immunogenic cell-associated peptide antigens (PA) such as those associated with cancers (i.e. self-proteins) (e.g. human PSM (undefined), Her2 and/or fibroblast growth factor (FGF) 8b), is new.
DETAILED DESCRIPTION - A method (I) for inducing an immune responses against weakly immunogenic or non-immunogenic polypeptide antigens (PAs) in animals (including humans), comprising effecting simultaneous presentation by antigen producing cells (APCs) of the animals immune system of:
(1) at least 1 CTL (cytotoxic T-lymphocyte) group derived from the PA and/or at least 1 B-cell group derived from the cell-associated PA; and
(2) at least 1 first T helper cell group (TH1 group) which is foreign to the animal.
INDEPENDENT CLAIMS are also included for the following:
(1) a method (II) for the selection of an immunogenic analog of a cell-associated PA that is weakly immunogenic or non-immunogenic which is capable of inducing an immune response in an animal against cell displaying MHC (major histocompatability complex) Class I (MHC-I) molecules bound to group derived from the cell-associated PA, comprising:
(A) identifying a subsequence of the amino acid sequence of the cell-associated PA which does not contain known or predicted CTL groups;
(B) preparing at least 1 punitively immunogenic analogs of the PA

by introducing at least 1 TH group foreign to the animal in a position within the subsequence identified in step (A); and

(C) selecting those analogs from step (B) which are verifiably capable of inducing a CTL response in the animal

(2) a method (III) for the preparation of a cell that produces analogs of cell-associated PAs, comprising introducing a nucleic acid encoding the analog into a vector and transforming a suitable host cell (III) with the vector;

(3) a method (IV) for preparing analogs of cell-associated PAs comprising culturing the transformed host cell (III) under conditions suitable for expression of the protein and recovering the PA analog from the culture;

(4) an analog (V) of human PSM (undefined) that is immunogenic in humans and comprises at least part of all known and predicted CTL and B-cell groups of PSM and includes at least 1 foreign TH group;

(5) an analog (VI) of Her2 that is immunogenic in humans and comprises at least part of all known and predicted CTL and B-cell groups of Her2 and includes at least 1 foreign TH group;

(6) an analog (VII) of human/murine FGF (fibroblast growth factor) 8b that is immunogenic in humans and comprises at least part of all known and predicted CTL and B-cell groups of FGF 8b and includes at least 1 foreign TH group;

(7) compositions comprising (V), (VI) and/or (VII) and an adjuvant;

(8) nucleic acids ((VIII)-(X)) encoding (V), (VI) and/or (VII);

(9) vectors ((XI)-(XIII)) comprising (VIII)-(X) (respectively);

(10) a transformed cell (XIV) comprising (XI)-(XIII);

(11) compositions for inducing production of antibodies against PSM, Her2 and FGF 8b, comprising (VIII)-(X) and/or (XI)-(XIII) and an adjuvant; and

(12) a method for the preparation of the cell (XIV), comprising transforming a host cell with (VIII)-(X) or (XI)-(XIII).

USE - (I) is used to stimulate immune responses to weakly, or non-immunogenic peptide antigens especially self proteins for the treatment of diseases associated with expression of those antigens. If the PA is human PSM (undefined), (I) is used for the treatment of prostate cancer . If the PA is human fibroblast growth factor (FGF) 8b, (I) is used for the treatment of prostate cancer or breast cancer . If the PA is Her2, (I) is used for the treatment of breast cancer (claimed).

pp; 219 DwgNo 0/6

2/AB/54 (Item 6 from file: 351)
DIALOG(R)File 351:Derwent WPI
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013131896
WPI Acc No: 2000-303767/200026
XRAM Acc No: C00-092286
Inhibiting endothelial cell growth and angiogenesis using calreticulin, useful for suppressing tumor growth
Patent Assignee: US DEPT HEALTH & HUMAN SERVICES (USSH)
Inventor: PIKE S E; TOSATO G; YAO L
Number of Countries: 089 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200020577	A1	20000413	WO 99US23240	A	19991005	200026	B
AU 9962917	A	20000426	AU 9962917	A	19991005	200036	

Priority Applications (No Type Date): US 98103438 A 19981006
Patent Details:

Patent No Kind Lan Pg Main IPC Filing Notes
WO 200020577 A1 E 93 C12N-015/11
Designated States (National): AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
AU 9962917 A C12N-015/11 Based on patent WO 200020577

Abstract (Basic): WO 200020577 A1
Abstract (Basic):

NOVELTY - A method (I) of inhibiting endothelial cell (EC) growth , comprising contacting the ECs with calreticulin (or fragments/variants), is new.

DETAILED DESCRIPTION - A method (I) of inhibiting endothelial cell (EC) growth , comprising contacting the ECs with a composition comprising:

(1) therapeutically active fragments of calreticulin ;
(2) therapeutically active variants of calreticulin ;
(3) calreticulin ; and/or
(4) therapeutically active variants of the fragments of (1).

INDEPENDENT CLAIMS are also included for the following:

(i) a protein (II) comprising an amino acid sequence selected from:
(A) at least 5 contiguous amino acids from a defined 400 amino acid (aa) sequence (Ia) given in the specification;
(B) at least 5 contiguous amino acids from a defined 180 aa sequence (Ib) given in the specification;
(C) at least 5 contiguous amino acids from a defined 61 aa sequence (Ic) given in the specification;
(D) at least 5 contiguous amino acids from a defined 49 aa sequence (Id) given in the specification;
(E) at least 5 contiguous amino acids from a defined 60 aa sequence (Ie) given in the specification; and/or
(F) at least 5 contiguous amino acids from a defined 280 aa sequence (If) given in the specification;
(ii) a vector (III) comprising a nucleotide sequence encoding (II);
(iii) a host cell (IV) comprising (III);
(iv) a method (V) of isolating an active fragment or variant of calreticulin from a sample comprising:
(A) contacting the sample with at least 1 peptide comprising one of 2 defined sequences given in the specification;
(B) recovering the portion of the sample that does not bind to the peptide; and
(C) assaying the recovered portion of the sample for therapeutic activity;
(v) an active fragment or variant (VI) of calreticulin identified by (V);
(vi) a vector (VII) encoding (VI);
(vii) a host (VIII) cell comprising (VII);
(viii) an active fragment or variant (IX) of calreticulin that:
(A) does not bind to a defined amino acid sequence given in the specification; and
(B) causes at least 30% inhibition of angiogenesis , tumor growth and/or EC growth;
(ix) a vector (X) encoding (IX);
(x) a host comprising (X); and
(xi) mimetics of (II), (VI) and (IX).

ACTIVITY - Anti-angiogenic; neuroprotective; antidiabetic; cytostatic; ophthalmic; dermalogical; immunosuppressive; antiinflammatory; anti-atherosclerotic; gastrointestinal;

anti-arthritic; hepatic.

MECHANISM OF ACTION - In (I), the calreticulin inhibits angiogenesis stimulated by an angiogenesis inducer (e.g. basic fibroblast growth factor, acidic fibroblast growth factor, vascular endothelial growth factor (VEGF), hepatocyte growth factor, interleukin (IL)-15, IL-8, platelet derived endothelial cell growth factor (PDECGF), transforming growth factor (TGF)-beta, tumor necrosis factor (TNF)-alpha, angiogenin and/or Cripto) (claimed).

Fragments of calreticulin causes at least 40% inhibition of angiogenesis , tumor growth and/or EC growth (claimed).

USE - Method (I) may be used for inhibiting angiogenesis in a patient. The angiogenesis is associated with a disease other than a tumor that is associated with neovascularization (e.g. diabetic neuropathy, retrolental fibroplasia, trachoma, neovascular glaucoma, psoriasis, angiofibromas, immmuninflammation, atherosclerosis, excessive wound repair, retinal neovascularization, macular degeneration, corneal graft rejection, contact lens overwear, Crohn's disease, non-immune inflammation, rheumatoid arthritis, systemic lupus erythromatosus, thyroiditis, Goodpasture's syndrome, systemic vasculitis, scleroderma, Sjorgen's syndrome, sarcoidosis and primary biliary cirrhosis). (I) may also be used for treating /inhibiting tumor growth especially Kaposi's sarcoma (claimed).

pp; 93 DwgNo 0/18

2/AB/55 (Item 7 from file: 351)
DIALOG(R)File 351:Derwent WPI
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012336747
WPI Acc No: 1999-142854/199912
XRAM Acc No: C99-041783
New peptides that bind calreticulin and modulate gene expression - are activated by hormone receptors, useful in the treatment of cancer, chronic inflammation and osteoporosis
Patent Assignee: DEDHAR S (DEDH-I); DOERSON C W (DOER-I); MAZUR A W (MAZU-I); DOERSEN C W (DOER-I)
Inventor: DEDHAR S; DOERSEN C W; MAZUR A W
Number of Countries: 083 Number of Patents: 004
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 9905172	A2	19990204	WO 98CA715	A	19980724	199912	B
AU 9885251	A	19990216	AU 9885251	A	19980724	199926	
EP 1001986	A2	20000524	EP 98936040	A	19980724	200030	
			WO 98CA715	A	19980724		
KR 2001022235	A	20010315	KR 2000700808	A	20000124	200159	

Priority Applications (No Type Date): US 97900241 A 19970724
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9905172	A2	E	64	C07K-014/47	

Designated States (National): AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

AU 9885251	A		C07K-014/47	Based on patent WO 9905172
EP 1001986	A2	E	C07K-014/47	Based on patent WO 9905172

Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

KR 2001022235 A C07K-014/00

Abstract (Basic): WO 9905172 A

New isolated and purified peptides (I) that bind to calreticulin (CR) comprise the sequence: KGX1X2X3R, where one or more of Xs = basic amino acid (aa). Also claimed are CR-binding peptides (Ia) containing one of the sequences KV(N-acylated)AFKR; K(V, G or A)FFKR; GGFF(K or R)R, (all D-amino acids); KGFFRR; KGFFRG; AVFFKR; KVFFAR; or KVAFKR.

USE - (I) and (Ia) are used to treat cancer (particularly of the prostate or breast, or promyelocytic leukaemia), chronic inflammation (e.g. arthritis) or osteoporosis (claimed), also they can be used to treat other bone diseases. (I) and (Ia) act by modulating binding of hormone receptors (HR) to DNA.

Dwg.0/4

2/AB/56 (Item 8 from file: 351)
DIALOG(R)File 351:Derwent WPI
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010946687
WPI Acc No: 1996-443637/199645
XRAM Acc No: C96-139680
Prod. comprising calreticulin or calreticulin-binding peptide - useful for modulating hormone responsiveness, esp. for treating e.g. cancer, osteoporosis or arthritis
Patent Assignee: DEDHAR S (DEDH-I)
Inventor: DEDHAR S
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
CA 2140814	A	19960724	CA 2140814	A	19950123	199645	B

Priority Applications (No Type Date): CA 2140814 A 19950123
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
CA 2140814	A		47	C12N-015/12	

Abstract (Basic): CA 2140814 A

An isolated and purified prod. for use in modulating hormone responsiveness is new.

USE - The prod. can be used for treating breast cancer , prostate cancer , promyelocytic leukaemia, solid tumours, chronic inflammatory diseases, arthritis and osteoporosis (claimed).

Dwg.0/3

2/AB/57 (Item 9 from file: 351)
DIALOG(R)File 351:Derwent WPI
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010865683
WPI Acc No: 1996-362634/199636
XRAM Acc No: C96-114243
Cpds esp. calreticulin, its mimetics or binding peptides for modulating hormone responsiveness - and treating diseases, e.g. cancer, by regulating hormone-induced gene transcription.
Patent Assignee: DEDHAR S (DEDH-I); ST-ARNAUD R (STAR-I); ONTARIO CANCER TREATMENT & RES FOUND (ONTA-N); SHRINERS HOSPITALS FOR CHILDREN (SHRI-N)
Inventor: DEDHAR S; ST-ARNAUD R
Number of Countries: 067 Number of Patents: 007

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 9623001	A1	19960801	WO 95CA664	A	19951123	199636	B
AU 9539203	A	19960814	AU 9539203	A	19951123	199650	
			WO 95CA664	A	19951123		
EP 807121	A1	19971119	EP 95936911	A	19951123	199751	
			WO 95CA664	A	19951123		
US 5854202	A	19981229	US 95377432	A	19950124	199908	
KR 98701647	A	19980625	WO 95CA664	A	19951123	199924	
			KR 97705041	A	19970724		
AU 9945861	A	19991028	AU 9539203	A	19951123	200005	N
			AU 9945861	A	19990901		
JP 2000507801	W	20000627	WO 95CA664	A	19951123	200036	
			JP 96522508	A	19951123		

Priority Applications (No Type Date): US 95377432 A 19950124; AU 9945861 A 19990901

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9623001	A1	E	85	C07K-014/575	

Designated States (National): AL AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG US UZ VN

Designated States (Regional): AT BE CH DE DK ES FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG

AU 9539203	A		C07K-014/575	Based on patent WO 9623001
EP 807121	A1	E	C07K-014/575	Based on patent WO 9623001

Designated States (Regional): DE DK ES FR GB IT NL

US 5854202	A		C07K-007/00	
KR 98701647	A		C07K-014/5751	Based on patent WO 9623001
AU 9945861	A		C07K-014/575	Div ex application AU 9539203
JP 2000507801	W	86	C12N-015/09	Based on patent WO 9623001

Abstract (Basic): WO 9623001 A

Isolating and purified product (I) for modulating hormone responsiveness are new. Also new is DNA encoding (I).

USE - (I), esp. calreticulin (Ia), its mimetics and peptides that bind to it, inhibit or promote hormone receptor induced gene transcription, so can be used to treat diseases, esp. breast or prostate cancer , promyelocytic leukaemia, solid tumours, chronic inflammation, arthritis and bone disease (osteoporosis, osteopotrosis, osteogaenia, rickets, osteomalacia or osteodystrophy). DNA encoding (I) or (Ia) can be used in gene therapy.

Dwg.2C/10

2/AB/58 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs
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0266785 DBA Accession No.: 2001-06539
Use of bleomycin- and heat shock-induced calreticulin promoter for construction of a mammalian expression vector- potential protection of chemotherapy patient from immunological reaction against bleomycin
AUTHOR: Elmileik H; Kumagai T; Berengena M; Ueda K; +Sugiyama M
CORPORATE AFFILIATE: Univ.Hiroshima-Inst.Pharm.Sci.
CORPORATE SOURCE: Institute of Pharmaceutical Sciences, Faculty of Medicine, Hiroshima University, Kasumi 1-2-3, Minami-ku, Hiroshima 734-8551, Japan. email:sugi@hiroshima-u.ac.jp
JOURNAL: J.Biochem. (129, 5, 671-74) 2001
ISSN: 0021-924X CODEN: JOBIAO
LANGUAGE: English

ABSTRACT: Addition of bleomycin (Bm) to a NIH3T3 cell culture induced overproduction of 4 cellular proteins. 2 Of the proteins were identified on N-terminal protein sequence analysis as calreticulin and mitochondrial matrix protein P1, which are known heat shock proteins, respectively. The calreticulin promoter region was cloned from the genomic DNA of NIH3T3 cells and it was seen that heat shock treatment at 42 deg or addition of Bm to the NIH3T3 cells caused overexpression of the luciferase gene controlled by the cloned calreticulin promoter in plasmid pGL3-E/CP. This suggests that Bm induces the transcriptional activation of stress-heat shock genes. An expression vector, plasmid pcDNA/CP (6.4 kb) was constructed containing the calreticulin promoter for transfection of mammal cells. If the pcDNA/CP/blmA vector is expressed in lung tissue, the administered Bm will induce expression of calreticulin promoter-controlled blmA. The Bm-induced gene product may protect the lung tissues from the toxicity of Bm, used for malignancy chemotherapy. The vector may be used to protect patients from immunological cell response to the blmA protein. (15 ref)

2/AB/59 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs
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0254025 DBA Accession No.: 2000-08515 PATENT
Inhibiting endothelial cell growth and angiogenesis using calreticulin, useful for suppressing tumor growth- recombinant calreticulin production via vector-mediated gene transfer and expression in host cell for e.g. neovascular glaucoma, Crohn disease and psoriasis-related angiogenesis inhibition
AUTHOR: Tosato G; Pike S E; Yao L
CORPORATE SOURCE: Rockville, MD, USA.
PATENT ASSIGNEE: U.S.Dep.Health-Hum.Serv.; Nat.Inst.Health-Rockville 2000
PATENT NUMBER: WO 200020577 PATENT DATE: 20000413 WPI ACCESSION NO.: 2000-303767 (2026)
PRIORITY APPLIC. NO.: US 103438 APPLIC. DATE: 19981006
NATIONAL APPLIC. NO.: WO 99US23240 APPLIC. DATE: 19991005
LANGUAGE: English
ABSTRACT: A method (I) for inhibiting endothelial cell (EC) growth which consists of contacting the ECs with calreticulin or its fragments or variants, is new. Also claimed are: a protein (II) which consists of a protein sequence with at least 5 contiguous amino acids of a 400, 180, 61, 49, 60 or 280 amino acid protein sequence (all specified); a vector (III) containing a DNA sequence encoding (II); a host cell transformed with (III); and a method for isolating an active fragment of variant of calreticulin from a sample. The above may be useful for the recombinant production of calreticulin and the inhibition of angiogenesis associated with a disease other than a tumor, such as diabetic neuropathy, retrolental fibroplasia, trachoma, neovascular glaucoma, Crohn disease and psoriasis. (93pp)

2/AB/60 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs
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0203978 DBA Accession No.: 96-14749 PATENT
Product for modulating hormone responsiveness- recombinant calreticulin and mimetic production for use as hormone receptor-induced transcription- inhibitor in cancer, chronic inflammatory disease, etc., therapy; gene therapy

AUTHOR: Dedhar S
CORPORATE SOURCE: Canada.
PATENT ASSIGNEE: Dedhar S 1996
PATENT NUMBER: CA 2140814 PATENT DATE: 960724 WPI ACCESSION NO.: 96-443637 (9645)
PRIORITY APPLIC. NO.: CA 2140814 APPLIC. DATE: 950123
NATIONAL APPLIC. NO.: CA 2140814 APPLIC. DATE: 950123
LANGUAGE: English
ABSTRACT: A new method for modulating hormone responsiveness involves using a peptide (I), especially calreticulin or calreticulin -binding peptide. (I) is calreticulin or a calreticulin mimetic which inhibits hormone receptor-induced gene transcription and binds to the protein sequence KXFFYR, where X = G, A or V and Y = K or R. Alternatively, (I) is a synthetic peptide that promotes hormone receptor-induced gene transcription, especially comprising the KXFFYR sequence. KXFFYR is present in the DNA-binding domain and is critical for the DNA binding activity of a variety of hormone receptors. Also new are: DNA encoding (I) for use in regulating hormone responsiveness; and a method for disease therapy in a mammal, which involves regulating hormone receptor-induced gene transcription in a cell. The method is useful for mamma carcinoma, prostate carcinoma, promyelocytic leukemia, solid tumor, chronic inflammatory disease, arthritis or osteoporosis therapy. The DNA encodes calreticulin or a calreticulin mimetic and is useful in gene therapy. (47pp)

2/AB/61 (Item 4 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs
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0201469 DBA Accession No.: 96-12240 PATENT
Compounds especially calreticulin, its mimetics or binding peptides for modulating hormone responsiveness- recombinant calreticulin preparation, gene transfer and antisense oligonucleotide for use as retinoic acid-antagonist, retinoic acid-agonist, androgen-antagonist and androgen-agonist
AUTHOR: Dedhar S; St-Arnaud R
CORPORATE SOURCE: Richmond Hill, Ontario, Canada; St. Laurent, Quebec, Canada.
PATENT ASSIGNEE: Dedhar S; St-Arnaud R 1996
PATENT NUMBER: WO 9623001 PATENT DATE: 960801 WPI ACCESSION NO.: 96-362634 (9636)
PRIORITY APPLIC. NO.: US 377432 APPLIC. DATE: 950124
NATIONAL APPLIC. NO.: WO 95CA664 APPLIC. DATE: 951123
LANGUAGE: English
ABSTRACT: An isolated and purified product, preferably calreticulin , its mimetics or peptides that bind to it, inhibit or promote hormone receptor-induced gene transcription, for use in modulating hormone responsiveness is claimed. The hormone receptors consist of glucocorticoid receptor, minerolcorticoid receptor, androgen receptor, progesterone receptor, estrogen receptor, retinoic acid receptor, thyrotropin receptor, calciferol receptor and orphan receptors. Also claimed is the DNA encoding the product. The DNA may be used to treat disease, especially mamma carcinoma or prostate cancer, promyelocytic leukemia, solid tumors, chronic inflammation, arthritis and bone disease. For example, transient or stable over-expression of calreticulin by cDNA transfection results in the inhibition of nuclear hormone receptor-induced gene transcriptional activity. Furthermore, decreased expression of calreticulin by stable transfection of antisense calreticulin cDNA results in increased sensitivity of the cells to hormones due to the increased

transcriptional activity of the nuclear hormone receptor. (85pp)

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